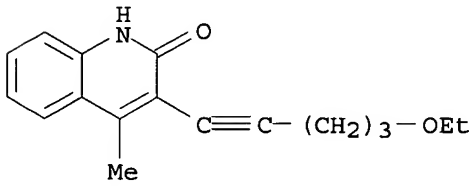
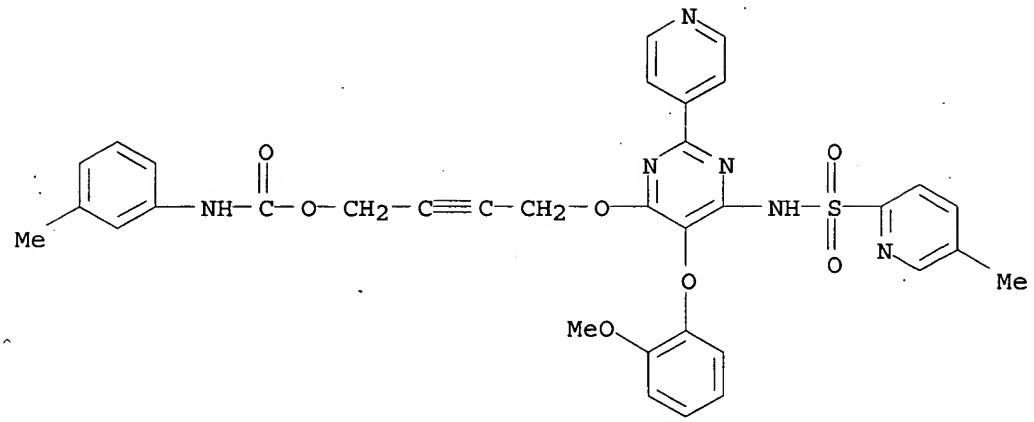
```
 * * * * * * * * * * * * STN  Columbus * * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 10:45:13 ON 14 MAY 2003

=> file reg

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=>
Uploading C:\STNEXP4\QUERIES\10055502.str

L1      STRUCTURE UPLOADED

=> que L1

L2    QUE L1

=> s l2
SAMPLE SEARCH INITIATED 10:45:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    1053 TO ITERATE

 95.0% PROCESSED     1000 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         19114 TO    23006
PROJECTED ANSWERS:              994 TO     2038

L3            50 SEA SSS SAM L1

=> d scan

L3    50 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN    2(1H)-Quinolinone, 3-(5-ethoxy-1-pentynyl)-4-methyl- (9CI)
MF    C17 H19 N O2
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3    50 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN    Carbamic acid, (3-methylphenyl)-, 4-[[5-(2-methoxyphenoxy)-6-[[(5-methyl-2-
      pyridinyl)sulfonyl]amino]-2-(4-pyridinyl)-4-pyrimidinyl]oxy]-2-butynyl
      ester (9CI)
```

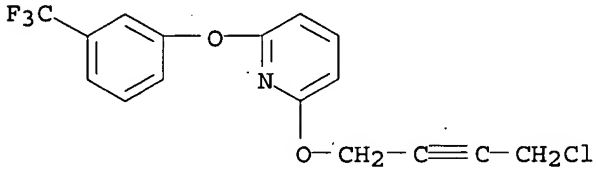
MF C34 H30 N6 O7 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 50 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Pyridine, 2-[(4-chloro-2-butynyl)oxy]-6-[3-(trifluoromethyl)phenoxy]-
(9CI)
MF C16 H11 Cl F3 N O2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1 sam
SAMPLE SEARCH INITIATED 10:46:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1053 TO ITERATE

95.0% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

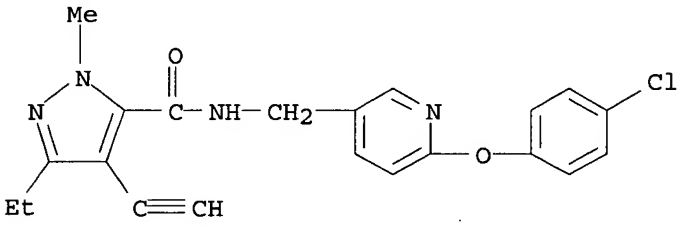
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 19114 TO 23006
PROJECTED ANSWERS: 994 TO 2038

L4 50 SEA SSS SAM L1

=> d scan

L4 50 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Pyrazole-5-carboxamide, N-[[6-(4-chlorophenoxy)-3-pyridinyl]methyl]-3-ethyl-4-ethynyl-1-methyl- (9CI)
MF C21 H19 Cl N4 O2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=> screen 1719

L5 SCREEN CREATED

=>
Uploading C:\STNEXP4\QUERIES\10055502.str

L6 STRUCTURE UPLOADED

=> que L6 AND L5

L7 QUE L6 AND L5

=> s l7 sam
SAMPLE SEARCH INITIATED 10:47:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

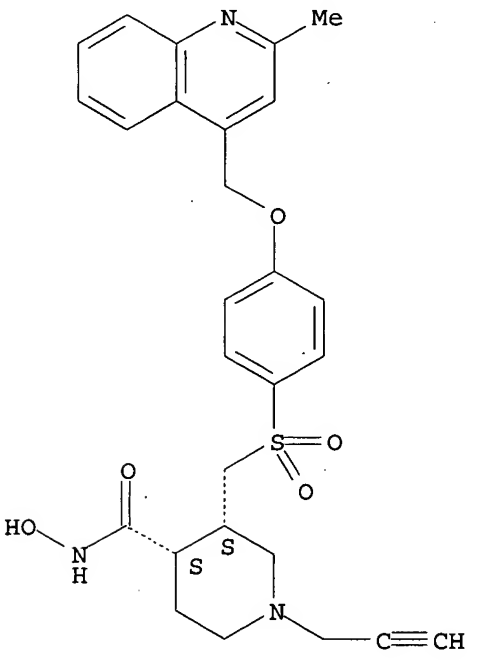
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 68 TO 532
PROJECTED ANSWERS: 1 TO 80

L8 1 SEA SSS SAM L6 AND L5

=> d scan

L8 1 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 4-Piperidinecarboxamide, N-hydroxy-3-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]sulfonyl]methyl]-1-(2-propynyl)-, (3S,4S)- (9CI)
MF C27 H29 N3 O5 S
CI COM

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s l7 full
FULL SEARCH INITIATED 10:47:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 290 TO ITERATE

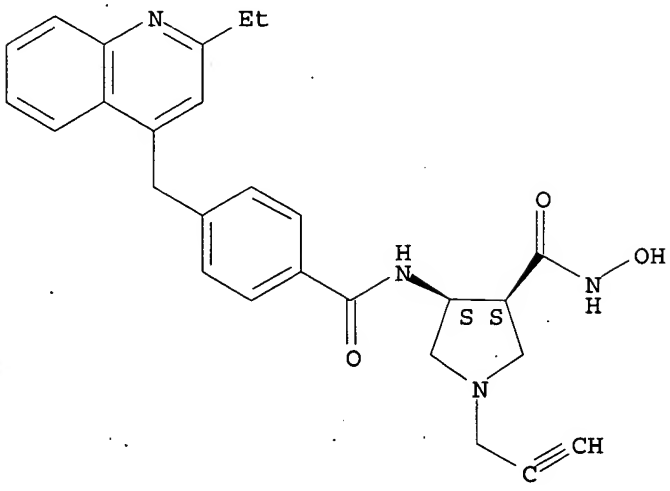
100.0% PROCESSED 290 ITERATIONS 51 ANSWERS
SEARCH TIME: 00.00.01

L9 51 SEA SSS FUL L6 AND L5

=> d scan

L9 51 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 3-Pyrrolidinecarboxamide, 4-[[4-[(2-ethyl-4-quinolinyl)methyl]benzoyl]amino]-N-hydroxy-1-(2-propynyl)-, (3S,4S)- (9CI)
MF C27 H28 N4 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file ca

=> s l9
L10 16 L9

=> d ibib abs hitstr 1-16

L10 ANSWER 1 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 138:271682 CA
TITLE: Preparation of cyclic hydroxamic acids as inhibitors of matrix metalloproteinases and/or TNF-.alpha. converting enzyme for treatment of inflammatory disorders
INVENTOR(S): Ott, Gregory; Chen, Xiao-Tao; Duan, Jingwu; Lu, Zhonghui
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

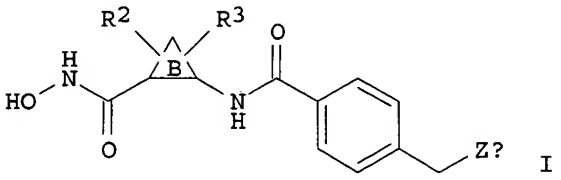
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024899	A2	20030327	WO 2002-US29685	20020916

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,

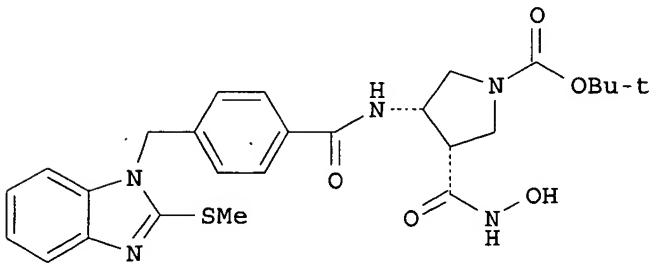
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-322630P P 20010917
OTHER SOURCE(S): MARPAT 138:271682

GI



I



II

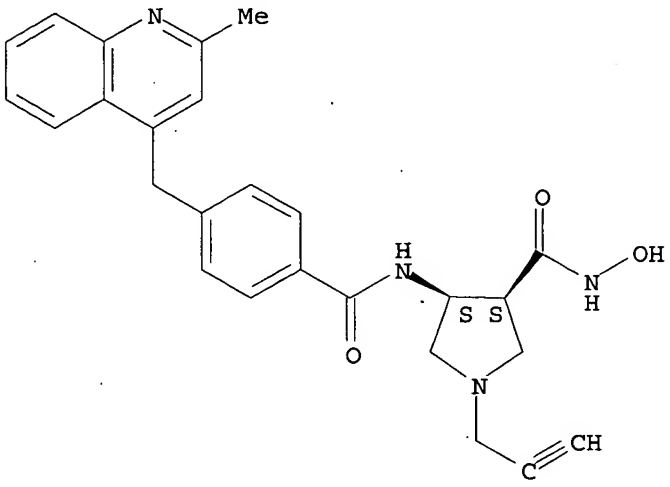
AB Title compds. I [wherein ring B = (un)substituted 4-7 membered (hetero)cyclic ring contg. 0-2 O, N, NR1, or SOp atoms and 0-3 carbonyl groups; R1 and R2 = independently Q, alk(en/yn)ylene-Q, or (un)substituted alkylene-Q interrupted by O, NRa, CO, CO2, CONRa, NRaCO, NRaCO2, NRaCONRa, SOp, NRaSO2, or SO2NRa; or R1 = (un)substituted alkylene-Q interrupted by OCO, OCO2, or OCONRa; Q = H or (un)substituted (hetero)cyclyl; R3 = Q1, Cl, F, alk(en/yn)ylene-Q1, or (un)substituted alkylene-Q1 interrupted by O, NR1, NRaCO, CONRa, CO, CO2, SOp, or SO2NRa; Q1 = H or (un)substituted Ph, naphthyl, or heterocyclyl; Za = (un)substituted benzimidazolyl, indolyl, imidazopyridinyl, pyrazolylpyridinyl, benzofuranyl, benzothiazinyl, quinolinyl, etc.; Ra = independently H, alkyl, Ph, or benzyl; p = 0-2; or stereoisomers or pharmaceutically acceptable salts thereof] were prepd. as inhibitors of matrix metalloproteinases (MMP), TNF-a converting enzyme (TACE), aggrecanase, or a combination thereof. For example, reaction of benzyl Me maleate with paraformaldehyde and glycine gave benzyl Me (cis)-3,4-pyrrolidinedicarboxlyate (100%). BOC-protection (64%), debenzylation (96%), resoln. of the (3S,4S)-isomer with (S)-.alpha.-methylbenzylamine, conversion to the carbamate with DPPA and PhCH2OH (76%), and Pd catalyzed hydrogenation (100%) provided Me (3S,4S)-4-amino-1-(tert-butoxycarbonyl)-3-pyrrolidinecarboxylate. Coupling of the amine with 4-[(2-methylthio-1H-benzimidazol-1-yl)methyl]benzoic acid (prepn. given) afforded the amide (99%), which was treated with NH2OH.bul.HCl/MeONa to give the hydroxamic acid (3S,4S)-II (33%). A no. of the compds. of the invention inhibited MMP-1, 2, 3, 7, 8, 9, 10, 12, 13, 14, 15, and/or 16 with Ki values of .ltoreq. 10 .mu.M. Thus, I are useful for the treatment of a wide variety of inflammatory disorders (no data).

IT **503169-64-0P 503169-65-1P 503169-81-1P 503169-82-2P 503170-68-1P 503170-71-6P**

503171-07-1P 503171-08-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MMR and/or TACE inhibitor; prepn. of cyclic hydroxamic acids as MMP and/or TACE inhibitors for treatment of inflammatory disorders)

RN 503169-64-0 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methyl]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

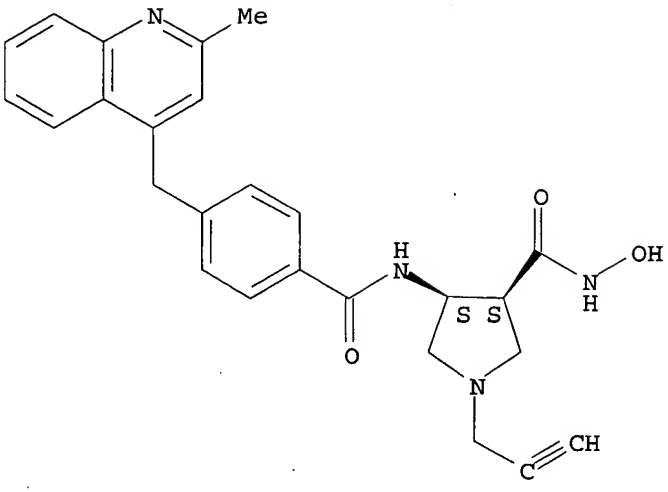


RN 503169-65-1 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methyl]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

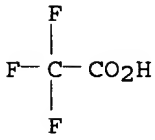
CRN 503169-64-0
CMF C26 H26 N4 O3

Absolute stereochemistry.



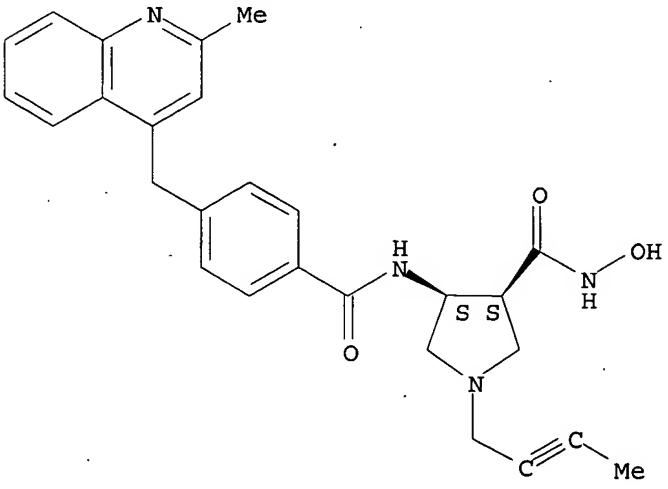
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 503169-81-1 CA
CN 3-Pyrrolidinecarboxamide, 1-(2-butynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methyl]benzoyl]amino]-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



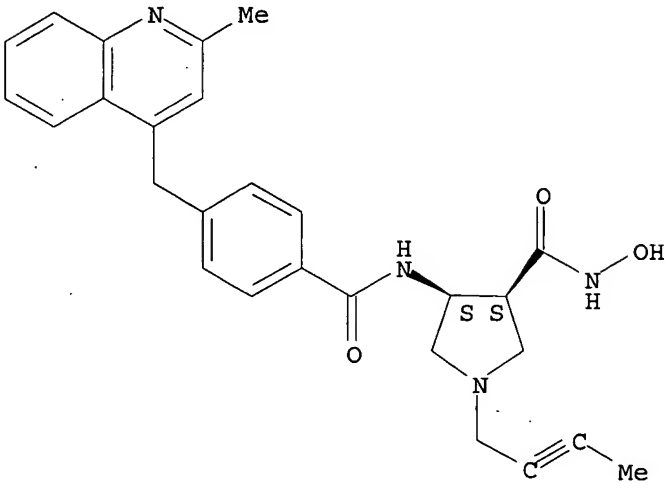
RN 503169-82-2 CA
CN 3-Pyrrolidinecarboxamide, 1-(2-butynyl)-N-hydroxy-4-[[4-[(2-methyl-4-

quinolinyl)methyl]benzoyl]amino]-, (3S,4S)-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

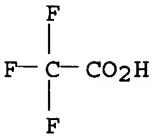
CRN 503169-81-1
CMF C27 H28 N4 O3

Absolute stereochemistry.



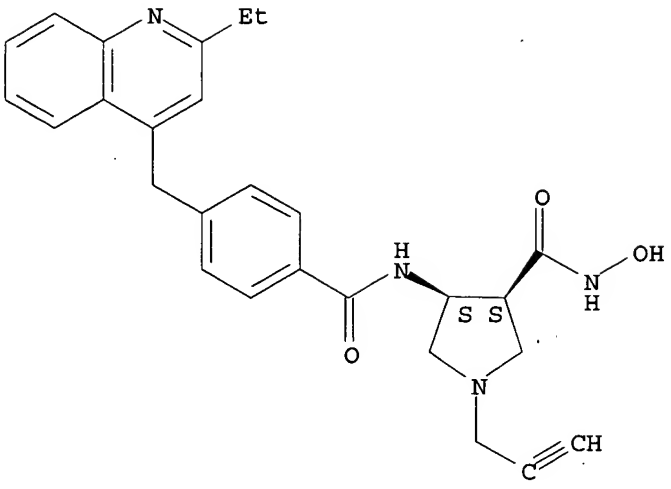
CM 2

CRN 76-05-1
CMF C2 H F3 O2



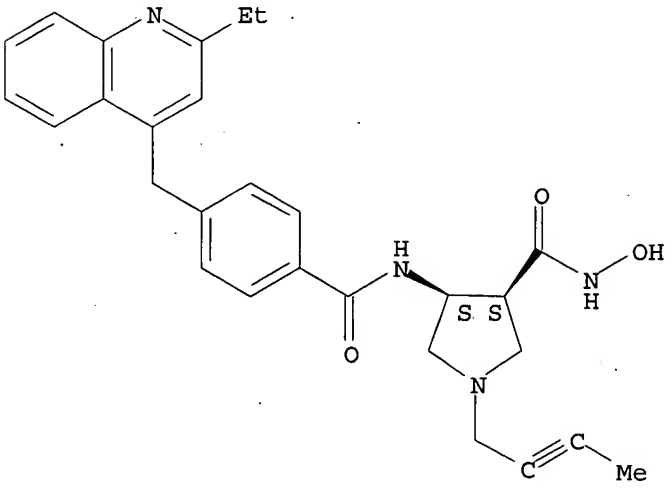
RN 503170-68-1 CA
CN 3-Pyrrolidinecarboxamide, 4-[[4-[(2-ethyl-4-quinolinyl)methyl]benzoyl]amino]-N-hydroxy-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



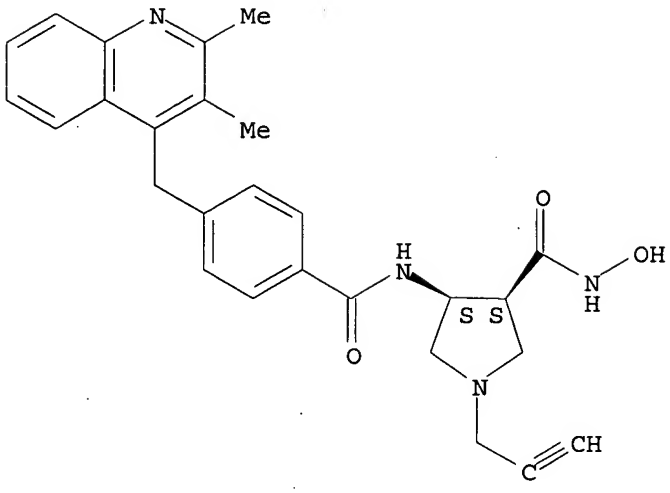
RN 503170-71-6 CA
CN 3-Pyrrolidinecarboxamide, 1-(2-butynyl)-4-[[4-[(2-ethyl-4-quinolinyl)methyl]benzoyl]amino]-N-hydroxy-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 503171-07-1 CA
CN 3-Pyrrolidinecarboxamide, 4-[[4-[(2,3-dimethyl-4-quinolinyl)methyl]benzoyl]amino]-N-hydroxy-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

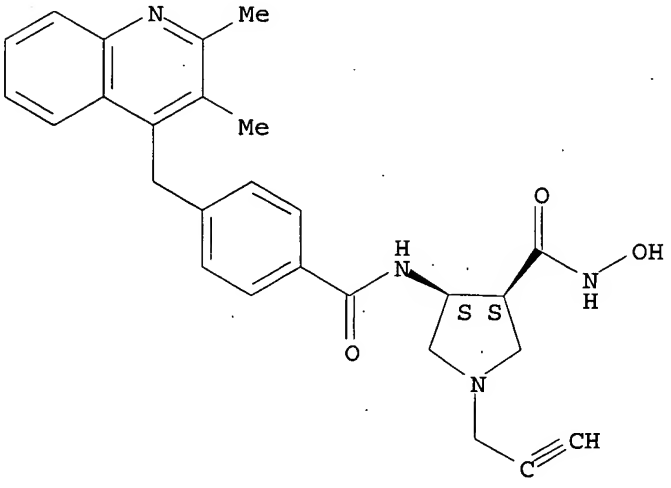


RN 503171-08-2 CA
CN 3-Pyrrolidinecarboxamide, 4-[[4-[(2,3-dimethyl-4-quinolinyl)methyl]benzoyl]amino]-N-hydroxy-1-(2-propynyl)-, (3S,4S)-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

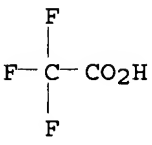
CRN 503171-07-1
CMF C27 H28 N4 O3

Absolute stereochemistry.



CM 2

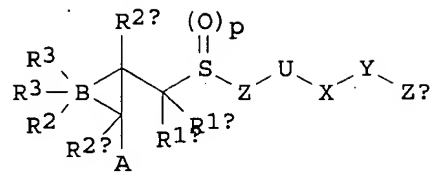
CRN 76-05-1
CMF C2 H F3 O2



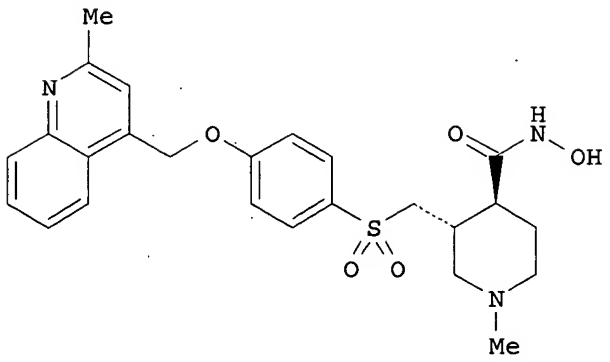
L10 ANSWER 2 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:93692 CA
TITLE: Preparation of (quinolinylmethoxyphenylsulfonylmethyl)-substituted pyrrolidinecarboxamides and piperidinecarboxamides as MMP, TNF, and/or aggrecanase inhibitors
INVENTOR(S): Xue, Chu-Biao; Decicco, Carl P.; He, Xiaohua
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company Patent Department, USA
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055491	A2	20020718	WO 2002-US760	20020109
WO 2002055491	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003087890	A1	20030508	US 2002-43541	20020109

PRIORITY APPLN. INFO.: US 2001-260957P P 20010111
OTHER SOURCE(S): MARPAT 137:93692
GI



I



II

AB Title compds. I [wherein A = COR5, CO2H, CH2CO2H, CO2R6, CONHOH, CONHOR5, CONHOR6, N(OH)CHO, N(OH)COR5, SH, CH2SH, SONHRa, SN2H2Ra, PO3H2, or PO(OH)NHRa; ring B = 3-10 membered (hetero)cycle; Z = absent or (un)substituted (hetero)cyclyl; U = absent or O, NH, N(alkyl),, CO, CO2, OCO, CONH, NHCO, OCO2, etc. X = absent or alkylene, alkenylene, or alkynylene; Y = absent or O, NH, N(alkyl), SO0-2, or CO; Za = (un)substituted (hetero)cyclyl; R1a and R1b = independently H, alkyl, Ph, PhCH2, CH2OR3, or (un)substituted CH2NH2; or CR1aR1b = (hetero)cyclyl; R2 = Q or (un)substituted alkylene-Q, alkenylene-Q, or alkynylene-Q, Q-substituted alkoxy(alkyl), carbamoyl(alkyl), sulfamoyl(alkyl), etc.; R2a = H, alkyl, ORa, (un)substituted CH2NH2, or SO0-2Ra; R2b = H or alkyl; Q = H or (un)substituted (hetero)cyclyl; R3 = Q1 or (un)substituted alkylene-Q1, alkenylene-Q1, or alkynylene-Q1, Q1-substituted alkoxy(alkyl), carbamoyl(alkyl), sulfamoyl(alkyl), etc.; or C(R3)2 = (un)substituted (hetero)cyclyl; Q1 = H or (un)substituted Ph, naphthyl, or heteroaryl; Ra = H, alkyl, Ph, or PhCH2; p = 0-2; R5 = (un)substituted alkyl; R6 = phenyl(alkyl), naphthyl, cycloalkyl, alkylcarbonyloxy, etc.; or pharmaceutically acceptable salt thereof] were prepd. as matrix metalloprotease (MMP), tumor necrosis factor (TNF), and aggrecanase inhibitors. For example, the 3-(quinolinylmethoxyphenylsulfonylmethyl)-4-piperidinecarboxamide (3R,4S)-II.bul.2CF3CO2H was prepd. in seventeen steps starting from the reaction of N-benzyloxycarbonyl-.beta.-alanine and benzylbromide. Key steps include the cyclization of the 5-aminopentanal intermediate and the addn. of 4-mercaptophenol and 4-chloromethyl-2-methylquinoline.bul.HCl. A no. of invention compds. exhibited Ki values of .ltoreq. 10 .mu.M against MMP-1, 2, 3, 9, and 13. Thus, I are useful for the treatment of inflammatory disorders and thromboembolic disorder (no data).

IT **441297-09-2P 441297-10-5P 441297-39-8P 441297-40-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

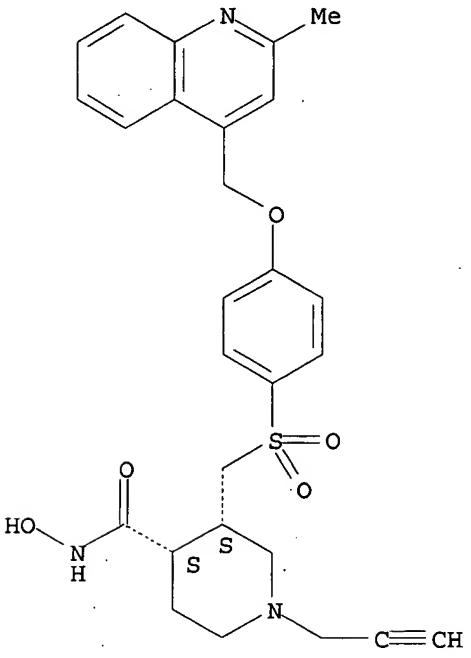
(MMP, TNF, and/or aggrecanase inhibitor; prepn. of (quinolinylmethoxyphenylsulfonylmethyl)-substituted

pyrrolidinecarboxamides and piperidinecarboxamides as MMP, TNF, and/or aggrecanase inhibitors)

RN 441297-09-2 CA

CN 4-Piperidinecarboxamide, N-hydroxy-3-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]sulfonyl]methyl]-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 441297-10-5 CA

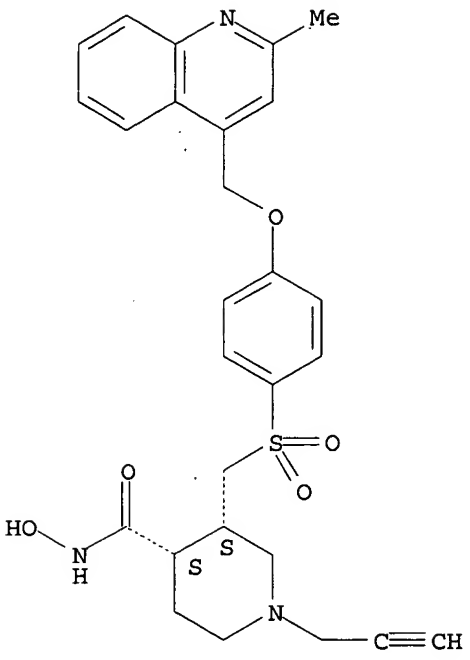
CN 4-Piperidinecarboxamide, N-hydroxy-3-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]sulfonyl]methyl]-1-(2-propynyl)-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 441297-09-2

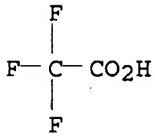
CMF C27 H29 N3 O5 S

Absolute stereochemistry.



CM 2

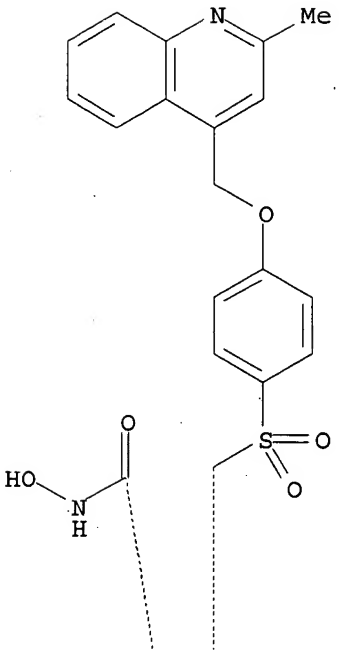
CRN 76-05-1
CMF C2 H F3 O2



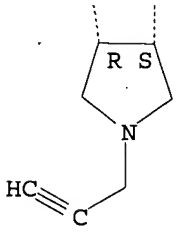
RN 441297-39-8 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]sulfonyl]methyl]-1-(2-propynyl)-, (3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



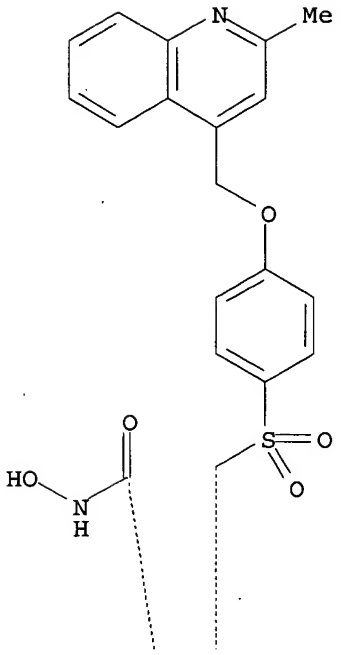
RN 441297-40-1 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]sulfonyl]methyl]-1-(2-propynyl)-, (3R,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

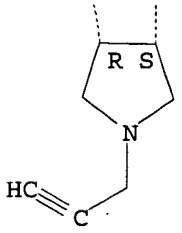
CRN 441297-39-8
CMF C26 H27 N3 O5 S

Absolute stereochemistry.

PAGE 1-A

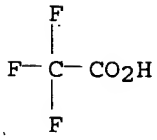


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



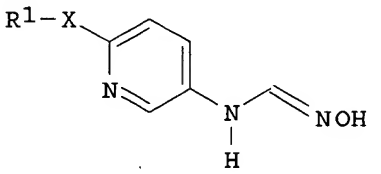
L10 ANSWER 3 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:37524 CA
TITLE: Preparation of pyridinylhydroxyformamidine derivatives as 20-HETE-producing enzyme inhibitors

INVENTOR(S): Sato, Masakazu; Miyata, Noriyuki; Ishii, Takaaki; Kobayashi, Yuko; Amada, Hideaki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096309	A1	20011220	WO 2001-JP5108	20010615
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2001074535	A5	20011224	AU 2001-74535	20010615
EP 1291343	A1	20030312	EP 2001-941061	20010615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

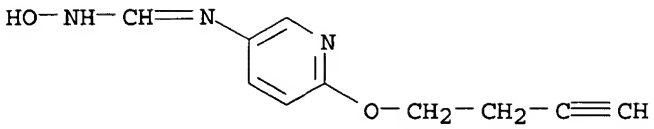
PRIORITY APPLN. INFO.:
JP 2000-180477 A 20000615
JP 2000-180479 A 20000615
JP 2000-336140 A 20001102
JP 2000-359781 A 20001127
WO 2001-JP5108 W 20010615

OTHER SOURCE(S): MARPAT 136:37524
GI

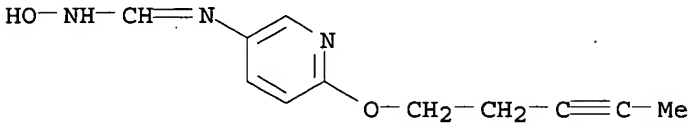


I

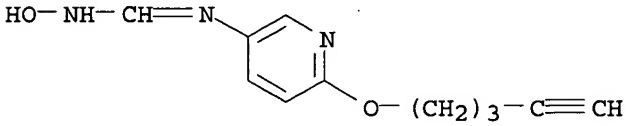
AB The title compds. I [R1 is a group of the general formula R2(CH2)m (wherein R2 is C3-8 cycloalkyl, C2-6 alkoxycarbonyl, C2-10 alkenyl, C2-6 alkynyl, optionally substituted aryl, or the like; and m is an integer of 1 to 8), a group of the general formula R3A (wherein R3 is hydrogen, C1-6 alkoxy, C3-8 cycloalkoxy, or the like; and A is linear C2-10 alkylene which may be substituted with C1-6 alkyl or trifluoromethyl), or C3-8 cycloalkyl; and X is oxygen or sulfur] are prepd. I are useful as remedies for kidney diseases, cerebrovascular diseases, etc. In an in vitro test using microsomes, N-[2-(3-dimethylamino-2,2-dimethylpropyl-1-oxy)pyridin-5-yl]-N'-hydroxyformamidine showed IC50 of 0.6 nM against 20-HETE prodn.
IT **380826-78-8P 380827-04-3P 380827-14-5P**
380827-23-6P 380827-78-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridinylhydroxyformamidine derivs. as 20-HETE-producing enzyme inhibitors)
RN 380826-78-8 CA
CN Methanimidamide, N-[6-(3-butynyloxy)-3-pyridinyl]-N'-hydroxy- (9CI) (CA INDEX NAME)



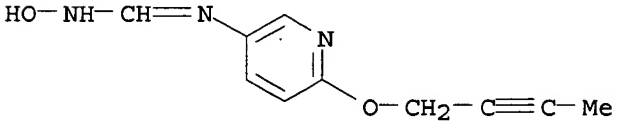
RN 380827-04-3 CA
CN Methanimidamide, N-hydroxy-N'-[6-(3-pentynyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)



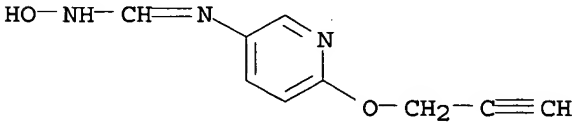
RN 380827-14-5 CA
CN Methanimidamide, N-hydroxy-N'-[6-(4-pentynyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)



RN 380827-23-6 CA
CN Methanimidamide, N-[6-(2-butynyloxy)-3-pyridinyl]-N'-hydroxy- (9CI) (CA INDEX NAME)



RN 380827-78-1 CA
CN Methanimidamide, N-hydroxy-N'-[6-(2-propynyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:272894 CA
TITLE: Preparation of .beta.-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-.alpha.
INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; Maduskuie, Thomas P., Jr.; Voss, Matthew E.

PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070734	A2	20010927	WO 2001-US8336	20010315
WO 2001070734	A3	20020314		
W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2001050850	A5	20011003	AU 2001-50850	20010315
EP 1263756	A2	20021211	EP 2001-924171	20010315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
US 2002013341	A1	20020131	US 2001-811116	20010316
US 6495565	B2	20021217		

PRIORITY APPLN. INFO.:

US 2000-190183P	P	20000317
US 2000-235467P	P	20000926
US 2000-252062P	P	20001120
WO 2001-US8336	W	20010315

OTHER SOURCE(S): MARPAT 135:272894

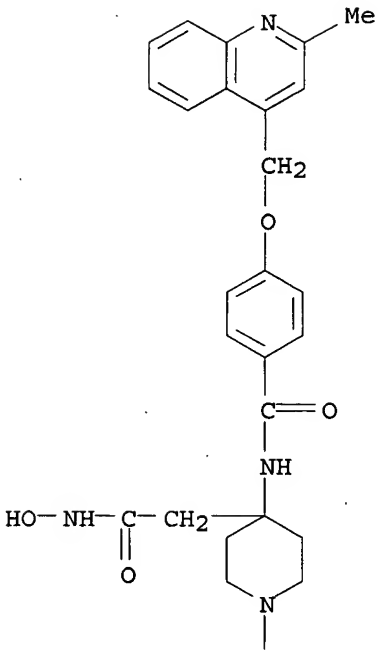
AB Novel .beta.-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepd. as metalloprotease and TNF-.alpha. inhibitors. Thus, N-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepd. by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

IT **362697-85-6P 362698-04-2P 362698-54-2P 362699-81-8P 362699-82-9P 362700-20-7P 362700-21-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-.alpha.)

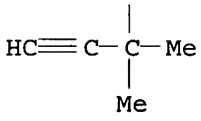
RN 362697-85-6 CA

CN 4-Piperidineacetamide, 1-(1,1-dimethyl-2-propynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

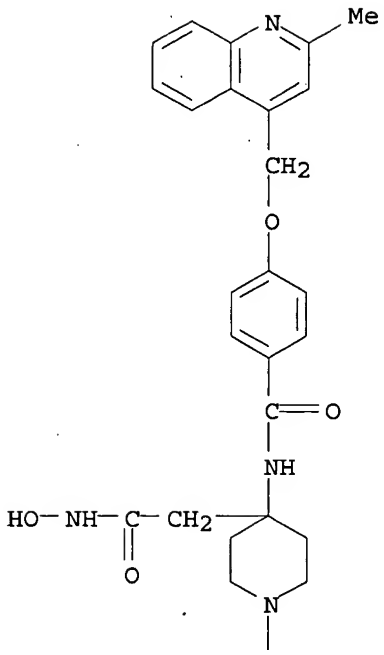


PAGE 2-A



RN 362698-04-2 CA
CN 4-Piperidineacetamide, N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



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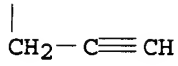
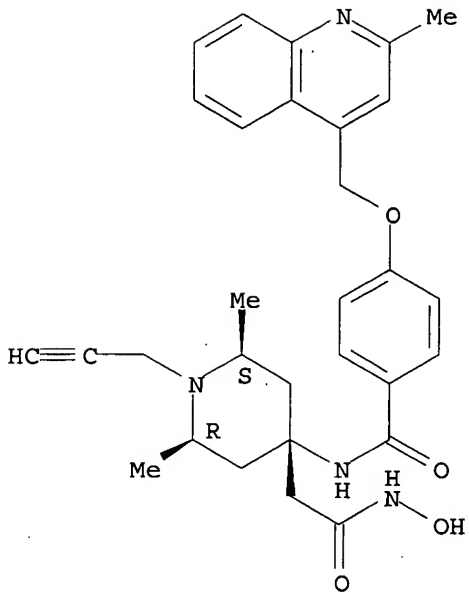
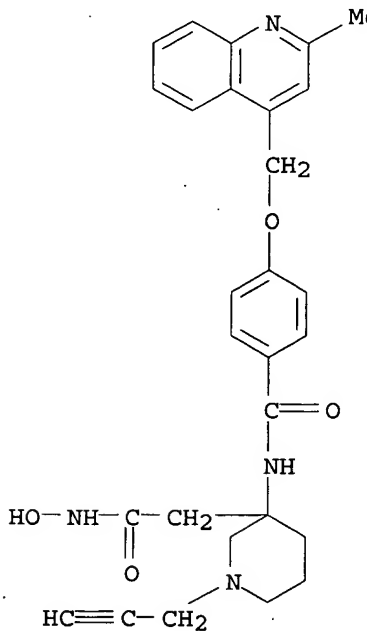


RN 362698-54-2 CA
CN 4-Piperidineacetamide, N-hydroxy-2,6-dimethyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, (2.alpha.,4.beta.,6.alpha.)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



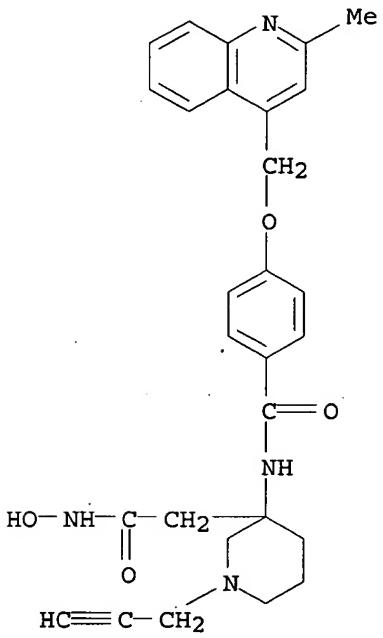
RN 362699-81-8 CA
CN 3-Piperidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)- (9CI) (CA INDEX NAME)



RN 362699-82-9 CA
CN 3-Piperidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

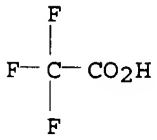
CM 1

CRN 362699-81-8
CMF C28 H30 N4 O4



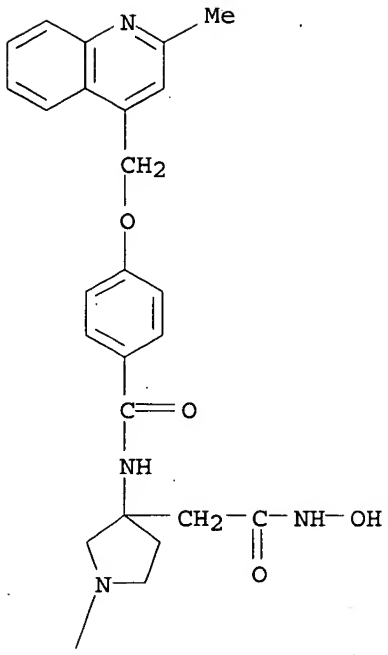
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 362700-20-7 CA
CN 3-Pyrrolidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



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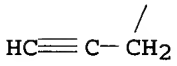
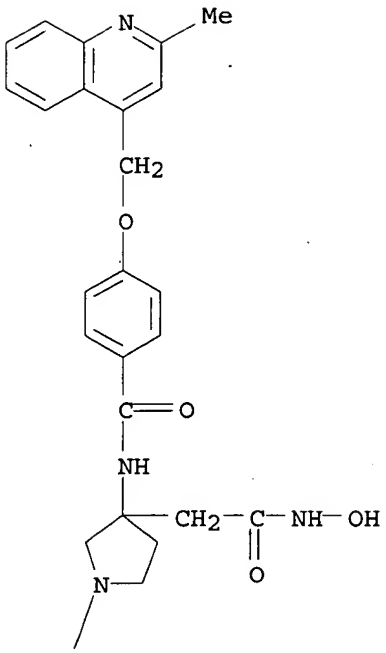


RN 362700-21-8 CA
CN 3-Pyrrolidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362700-20-7
CMF C27 H28 N4 O4

PAGE 1-A



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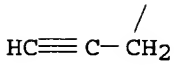
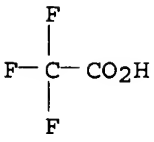


CM 2

CRN 76-05-1
CMF C2 H F3 O2



L10 ANSWER 5 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:257169 CA
TITLE: Preparation of cyclic .beta.-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-.alpha.
INVENTOR(S): Duan, Jingwu; Ott, Gregory; Chen, Linhua; Lu, Zhonghui; Maduskuie, Thomas P., Jr.; Voss, Matthew E.; Xue, Chu-Biao
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 298 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070673	A2	20010927	WO 2001-US8334	20010315
WO 2001070673	A3	20020314		
W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, HU, IN, JP, KR, LT, LU, LV, MX, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1263755	A2	20021211	EP 2001-924170	20010315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
US 2002016336	A1	20020207	US 2001-811233	20010316

PRIORITY APPLN. INFO.:
US 2000-190182P P 20000317
US 2000-233373P P 20000918
US 2000-255539P P 20001214
WO 2001-US8334 W 20010315

OTHER SOURCE(S): MARPAT 135:257169

AB Novel cyclic .beta.-amino acid derivs. A-CRR2aCRR2bNR1CO-Z-Ua-Xa-Ya-Za [A = CO2H, CH2CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl, Ph, benzyl), P(O)(OH)2, etc.; CRCR is a substituted 3-13 membered nonarom. carbocyclic or heterocyclic ring; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 (Ra1 = H, alkyl), CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Xa is absent or C1-10 alkylene, C2-10 alkenylene or alkynylene; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, C1-4 alkyl, Ph, benzyl; R2a is H, C1-6 alkyl, ORa, NRaRa1 or S(O)pRa; R2b is H, C1-6 alkyl (with provisos)] or pharmaceutically acceptable salts were prepd. as metalloprotease and TNF-.alpha. inhibitors. Thus, (3S,4S)-N-hydroxy-1-isopropyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-3-pyrrolidinecarboxamide was prepd. by a multistep procedure starting with condensation of benzyl Me maleate, glycine, and paraformaldehyde to form 3,4-pyrroledicarboxylate diester and involving amidation of 4-[(2-methyl-4-quinolinyl)methoxy]benzoic acid.

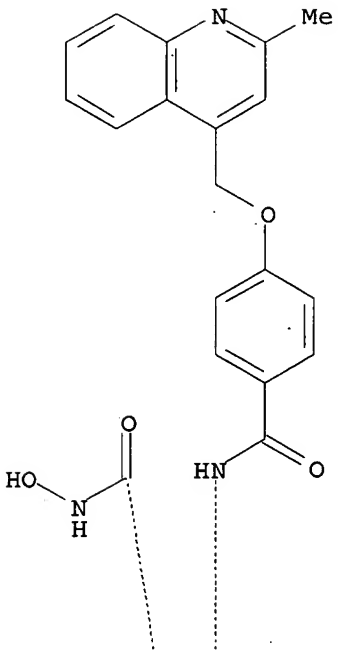
IT **362484-30-8P 362484-31-9P 362484-32-0P**
362484-33-1P 362484-54-6P 362484-55-7P
362485-03-8P 362485-04-9P 362485-05-0P
362485-06-1P 362487-19-2P 362487-20-5P
362488-05-9P 362488-06-0P 362488-11-7P
362488-12-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic .beta.-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-.alpha.)

RN 362484-30-8 CA

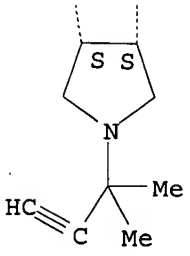
CN 3-Pyrrolidinecarboxamide, 1-(1,1-dimethyl-2-propynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



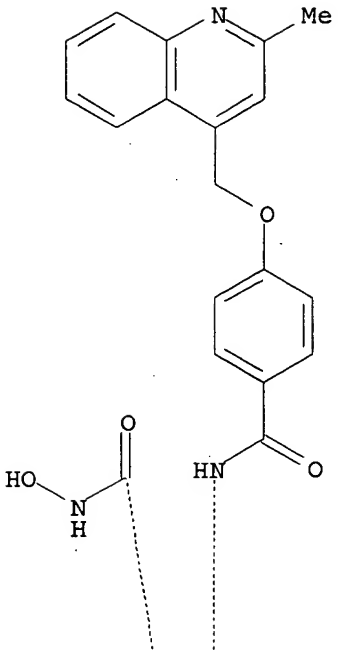
RN 362484-31-9 CA
CN 3-Pyrrolidinecarboxamide, 1-(1,1-dimethyl-2-propynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362484-30-8
CMF C28 H30 N4 O4

Absolute stereochemistry.

PAGE 1-A



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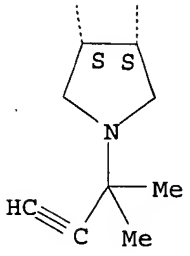
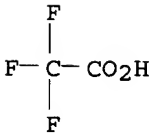


CM 2

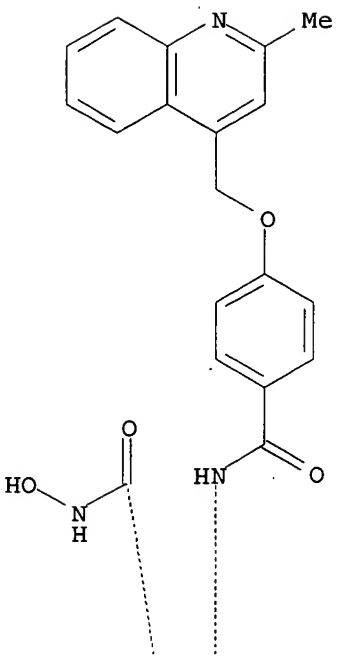
CRN 76-05-1
CMF C2 H F3 O2



RN 362484-32-0 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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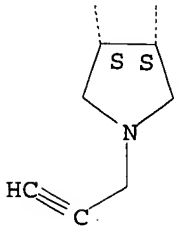


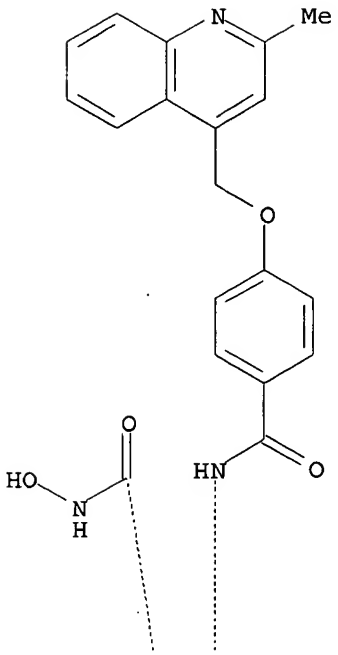
RN 362484-33-1 CA
CN 3-Pyrrolidinecarboxamide, N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362484-32-0
CMF C26 H26 N4 O4

Absolute stereochemistry.

PAGE 1-A



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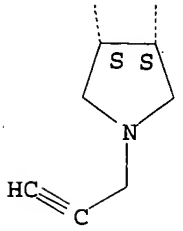
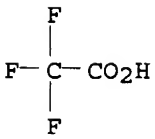


CM 2

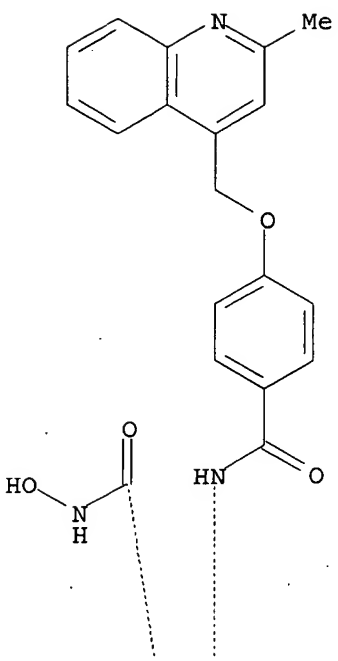
CRN 76-05-1
CMF C2 H F3 O2



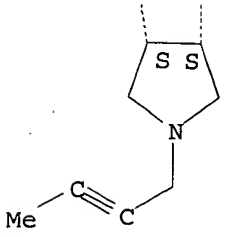
RN 362484-54-6 CA
CN 3-Pyrrolidinecarboxamide, 1-(2-butynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



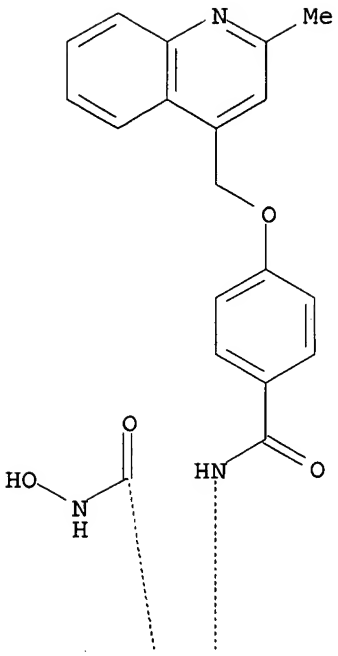
RN 362484-55-7 CA
CN 3-Pyrrolidinecarboxamide, 1-(2-butynyl)-N-hydroxy-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

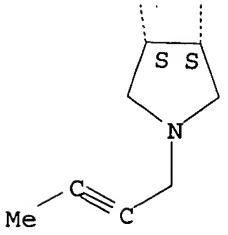
CRN 362484-54-6
CMF C27 H28 N4 O4

Absolute stereochemistry.

PAGE 1-A

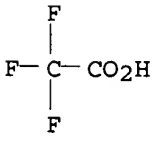


PAGE 2-A



CM 2

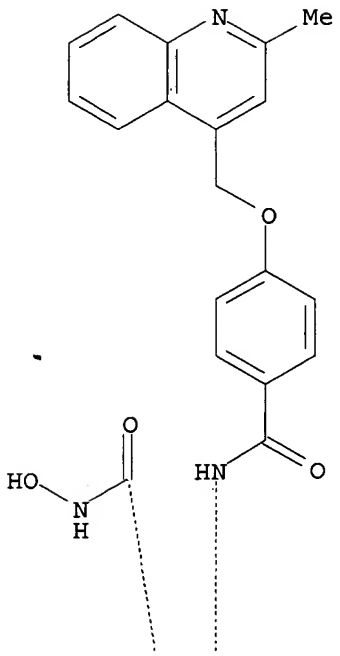
CRN 76-05-1
CMF C2 H F3 O2



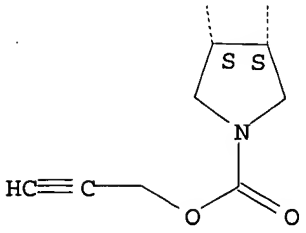
RN 362485-03-8 CA
CN 1-Pyrrolidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 2-propynyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



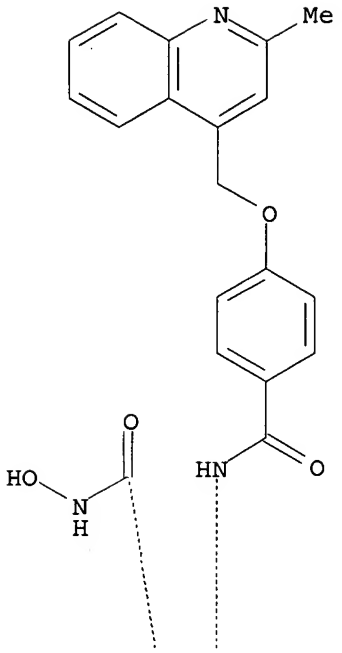
RN 362485-04-9 CA
CN 1-Pyrrolidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 2-propynyl ester, (3S,4S)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

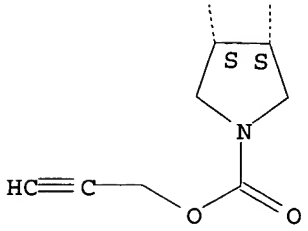
CRN 362485-03-8
CMF C27 H26 N4 O6

Absolute stereochemistry.

PAGE 1-A

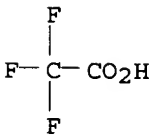


PAGE 2-A



CM 2

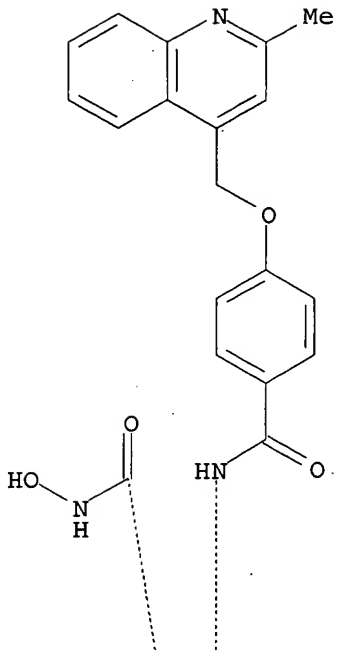
CRN 76-05-1
CMF C2 H F3 O2



RN 362485-05-0 CA
CN 1-Pyrrolidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 2-butynyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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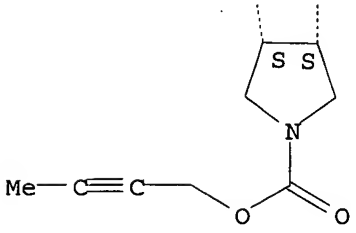


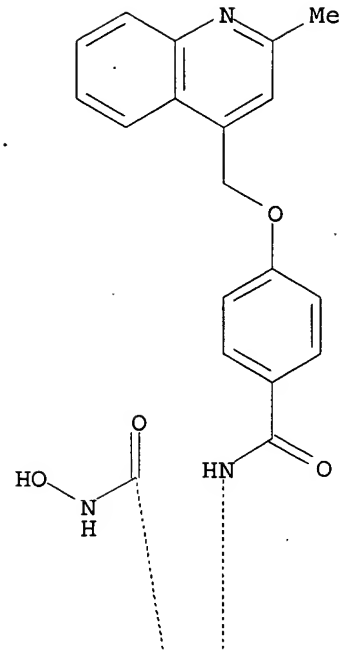
RN 362485-06-1 CA
CN 1-Pyrrolidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 2-butynyl ester, (3S,4S)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362485-05-0
CMF C28 H28 N4 O6

Absolute stereochemistry.

PAGE 1-A



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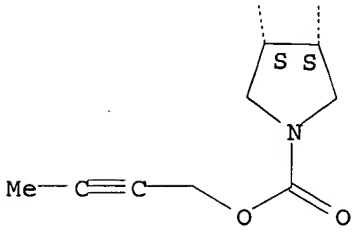
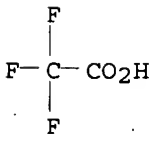


CM 2

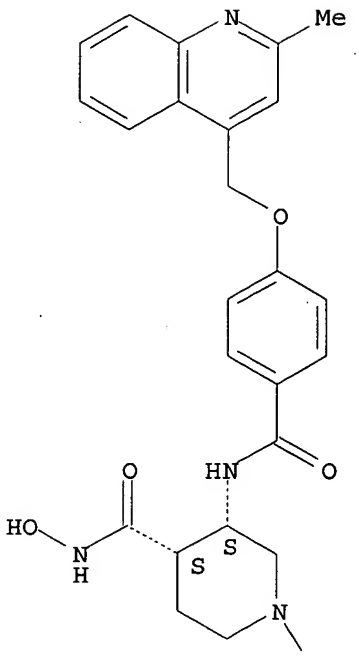
CRN 76-05-1
CMF C2 H F3 O2



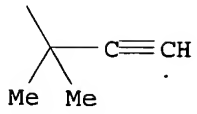
RN 362487-19-2 CA
CN 4-Piperidinecarboxamide, 1-(1,1-dimethyl-2-propynyl)-N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



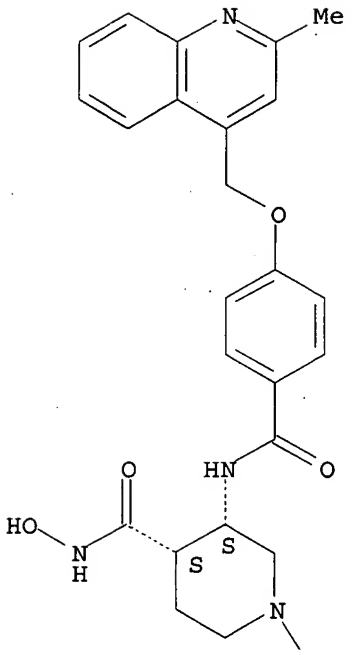
RN 362487-20-5 CA
CN 4-Piperidinecarboxamide, 1-(1,1-dimethyl-2-propynyl)-N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362487-19-2
CMF C29 H32 N4 O4

Absolute stereochemistry.

PAGE 1-A



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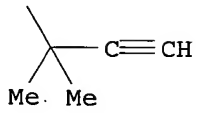
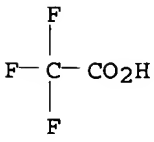


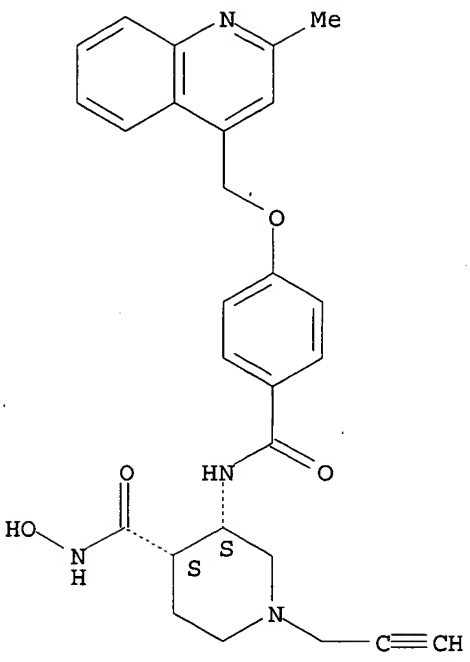
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 362488-05-9 CA
CN 4-Piperidinecarboxamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

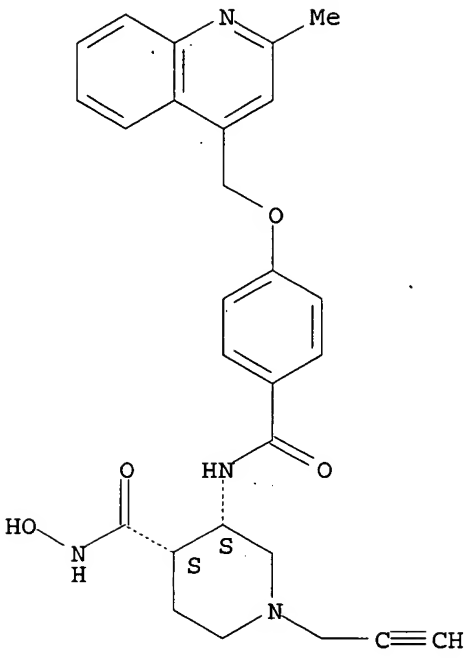


RN 362488-06-0 CA
CN 4-Piperidinecarboxamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-1-(2-propynyl)-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

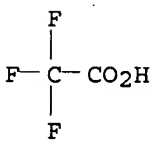
CRN 362488-05-9
CMF C27 H28 N4 O4

Absolute stereochemistry.



CM 2

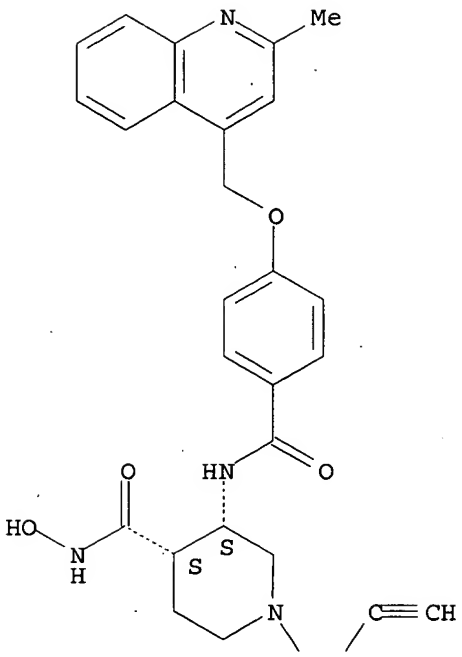
CRN 76-05-1
CMF C2 H F3 O2



RN 362488-11-7 CA
CN 4-Piperidinecarboxamide, N-hydroxy-1-(1-methyl-2-propynyl)-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

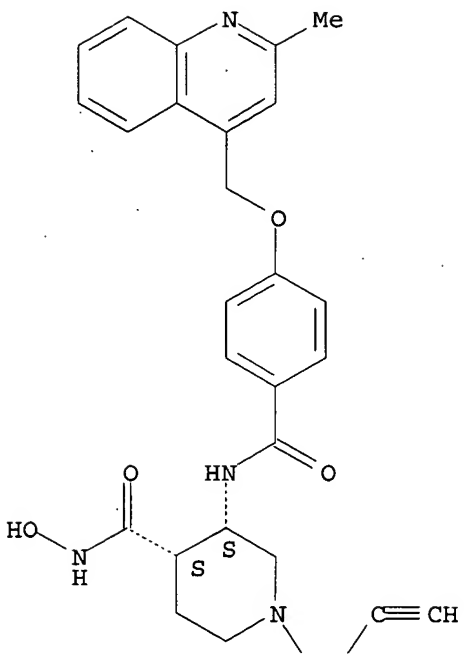
RN 362488-12-8 CA
CN 4-Piperidinecarboxamide, N-hydroxy-1-(1-methyl-2-propynyl)-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362488-11-7
CMF C28 H30 N4 O4

Absolute stereochemistry.

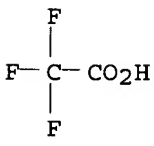
PAGE 1-A



PAGE 2-A

CM 2

CRN 76-05-1
CMF C2 H F3 O2



L10 ANSWER 6 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:326767 CA
TITLE: Preparation of acetylenic .alpha.-amino acid-based sulfonamide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy I.; Chen, James M.; Cole, Derek C.; Du, Mila T.; Laakso, Leif M.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: U.S., 109 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

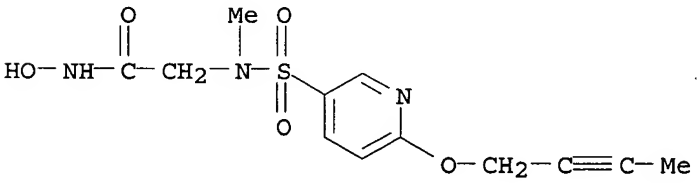
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6225311	B1	20010501	US 2000-492691	20000127
US 2003008849	A1	20030109	US 2000-748912	20001227

PRIORITY APPLN. INFO.: US 1999-155249P P 19990127
US 2000-492691 A3 20000127
OTHER SOURCE(S): MARPAT 134:326767

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepd. as inhibitors of TNF-.alpha. converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepd. and showed IC50 = 7.4 nM for inhibition of TACE.

IT **287404-21-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acetylenic .alpha.-amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

RN 287404-21-1 CA
CN Acetamide, 2-[[[6-(2-butynyloxy)-3-pyridinyl]sulfonyl]methylamino]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:237395 CA
TITLE: Preparation of heteroaryl acetylenic sulfonamide and phosphinic acid amide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy I.; Chen, James M.; Nelson, Frances C.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6200996	B1	20010313	US 2000-492976	20000127
US 2002188132	A1	20021212	US 2000-999908	20001204

PRIORITY APPLN. INFO.: US 1999-155229P P 19990127
US 2000-492976 A3 20000127

OTHER SOURCE(S): MARPAT 134:237395

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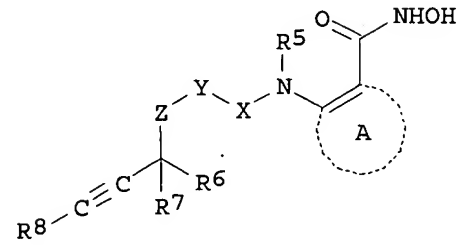

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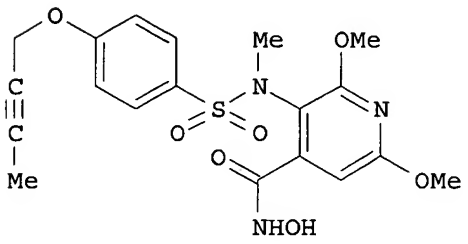


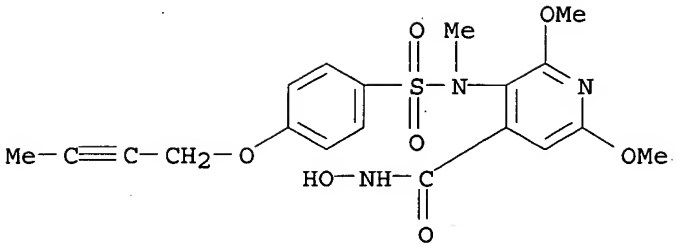
II

AB The title compds. [I; the CONHOH and NR5 moieties are bonded to adjacent carbons of group A; A = 5-6 membered heteroaryl having 1-3 heteroatoms selected from N, NR9, S, O; X = SO2, POR10; Y = aryl, 5-10 membered mono- or bicyclic heteroaryl having from 1-3 heteroatoms selected from N, NR9, S and O; with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R5 = H, alkyl; R6, R7 = H, alkyl, CN, C.tplbond.CH; R8 = H, alkyl, alkenyl, etc.; R9 = H, aryl, alkyl, etc.; R10 = alkyl, cycloalkyl, aryl, etc.], useful in treating disease conditions mediated by TNF-.alpha. such as rheumatoid arthritis, osteoarthritis, sepsis, AIDS, ulcerative colitis, multiple sclerosis, Crohn's disease and degenerative cartilage loss, were prepd. E.g., a multi-step synthesis of II which showed IC50 of 11 nM against TACE, and IC50 of 478 nM against MMP-13, was given.

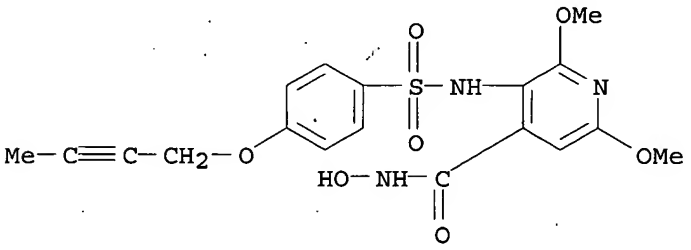
IT **286839-92-7P 286839-94-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl acetylenic sulfonamide and phosphinic acid amide hydroxamic acid TACE inhibitors)

RN 286839-92-7 CA

CN 4-Pyridinecarboxamide, 3-[[[4-(2-butynyloxy)phenyl]sulfonyl]methylamino]-N-hydroxy-2,6-dimethoxy- (9CI) (CA INDEX NAME)



RN 286839-94-9 CA
CN 4-Pyridinecarboxamide, 3-[[[4-(2-butynyloxy)phenyl]sulfonyl]amino]-N-hydroxy-2,6-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

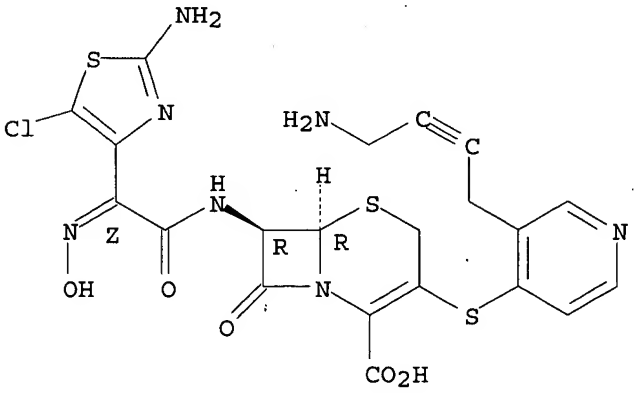
L10 ANSWER 8 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:141355 CA
TITLE: Discovery of RWJ-54428 (MC-02,479), a new cephalosporin active against resistant gram-positive bacteria
AUTHOR(S): Hecker, Scott J.; Glinka, Tomasz W.; Cho, Aesop; Zhang, Zhijia J.; Price, Mary E.; Chamberland, Suzanne; Griffith, David; Lee, Ving J.
CORPORATE SOURCE: Microcide Pharmaceuticals, Inc., Mountain View, CA, 94043, USA
SOURCE: Journal of Antibiotics (2000), 53(11), 1272-1281
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:141355

AB The discovery of RWJ-54428 (MC-02,479), a new cephalosporin displaying promising activity against sensitive and resistant Gram-pos. bacteria, is described. Progressive structural modification from the previously reported 3-phenylthiocephem MC-02,331 afforded an overall increase in potency against MRSA while retaining other key properties such as acceptable soly. and serum binding. Evaluation of the in vitro potency and in vivo efficacy of a series of closely related compds. resulted in selection of RWJ-54428 (MC-02,479) for further studies.

IT **189448-99-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(discovery of RWJ-54428 (MC-02,479), a new cephalosporin active against resistant gram-pos. bacteria)
RN 189448-99-5 CA

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[3-(4-amino-2-butynyl)-4-pyridinyl]thio]-7-[[(2Z)-(2-amino-5-chloro-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

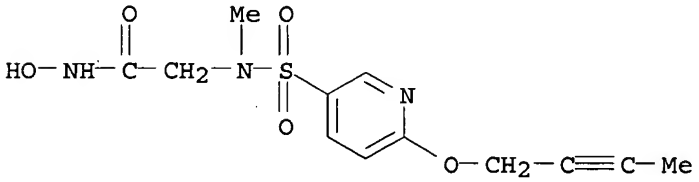


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:150908 CA
TITLE: Preparation of acetylenic .alpha.-amino acid-based sulfonamide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Cole, Derek Cecil
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044709	A2	20000803	WO 2000-US1981	20000127
WO 2000044709	A3	20001221		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356299	AA	20000803	CA 2000-2356299	20000127
EP 1144368	A2	20011017	EP 2000-905750	20000127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007752	A	20011204	BR 2000-7752	20000127
JP 2002535382	T2	20021022	JP 2000-595966	20000127
NO 2001003674	A	20010924	NO 2001-3674	20010726

BG 105738 A 20020531 BG 2001-105738 20010726
PRIORITY APPLN. INFO.: US 1999-238255 A 19990127
WO 2000-US1981 W 20000127
OTHER SOURCE(S): MARPAT 133:150908
AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepd. as inhibitors of TNF-.alpha. converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepd. and showed IC50 = 7.4 nM for inhibition of TACE.
IT **287404-21-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acetylenic .alpha.-amino acid-based sulfonamide hydroxamic acid TACE inhibitors)
RN 287404-21-1 CA
CN Acetamide, 2-[[[6-(2-butynyloxy)-3-pyridinyl]sulfonyl]methylamino]-N-hydroxy- (9CI) (CA INDEX NAME)

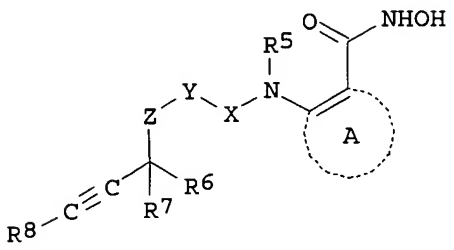


L10 ANSWER 10 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:135230 CA
TITLE: Preparation of heteroaryl acetylenic sulfonamide and phosphinic acid amide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Nelson, Frances Christy
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044740	A2	20000803	WO 2000-US1980	20000127
WO 2000044740	A3	20010125		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2356481 AA 20000803 CA 2000-2356481 20000127
EP 1147102 A2 20011024 EP 2000-913263 20000127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
BR 2000007726 A 20011030 BR 2000-7726 20000127
JP 2002535399 T2 20021022 JP 2000-595996 20000127
NO 2001003681 A 20010726 NO 2001-3681 20010726
PRIORITY APPLN. INFO.: US 1999-239091 A 19990127
WO 2000-US1980 W 20000127
OTHER SOURCE(S): MARPAT 133:135230
GI



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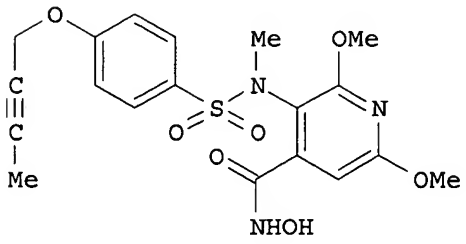


II

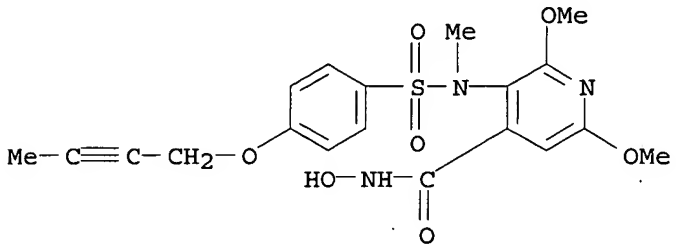
AB The title compds. [I; the CONHOH and NR5 moieties are bonded to adjacent carbons of group A; A = 5-6 membered heteroaryl having 1-3 heteroatoms selected from N, NR9, S, O; X = SO2, POR10; Y = aryl, 5-10 membered mono- or bicyclic heteroaryl having from 1-3 heteroatoms selected from N, NR9, S and O; with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R5 = H, alkyl; R6, R7 = H, alkyl, CN, CCH; R8 = H, alkyl, alkenyl, etc.; R9 = H, aryl, alkyl, etc.; R10 = alkyl, cycloalkyl, aryl, etc.], useful in treating disease conditions mediated by TNF-.alpha. such as rheumatoid arthritis, osteoarthritis, sepsis, AIDS, ulcerative colitis, multiple sclerosis, Crohn's disease and degenerative cartilage loss, were prepd. E.g., a multi-step synthesis of II which showed IC50 of 11 nM against TACE, and IC50 of 478 nM against MMP-13, was given.

IT **286839-92-7P 286839-94-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heteroaryl acetylenic sulfonamide and phosphinic acid amide hydroxamic acid TACE inhibitors)

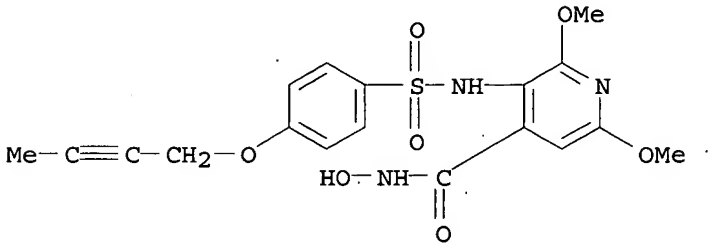
RN 286839-92-7 CA

CN 4-Pyridinecarboxamide, 3-[[[4-(2-butynyloxy)phenyl]sulfonyl]methylamino]-N-hydroxy-2,6-dimethoxy- (9CI) (CA INDEX NAME)



RN 286839-94-9 CA

CN 4-Pyridinecarboxamide, 3-[[[4-(2-butynyloxy)phenyl]sulfonyl]amino]-N-hydroxy-2,6-dimethoxy- (9CI) (CA INDEX NAME)



L10 ANSWER 11 OF 16 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 132:180424 CA

TITLE: Preparation of cephalosporin antibiotics

INVENTOR(S): Cho, In-Seop; Hecker, Scott J.; Glinka, Tomasz W.; Lee, Ving J.; Zhang, Zhijia J.

PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA

SOURCE: U.S., 41 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6030965	A	20000229	US 1997-940508	19970930

PRIORITY APPLN. INFO.: US 1997-940508 19970930

OTHER SOURCE(S): MARPAT 132:180424

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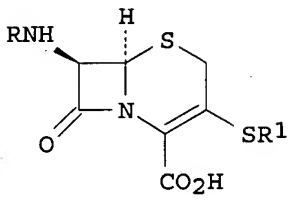

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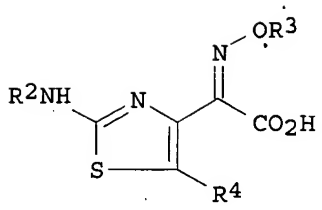
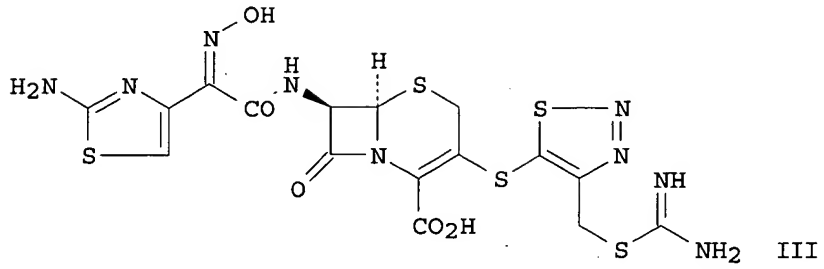


II



III

AB Cephalosporins, such as I [R = acyl; R1 = heterocyclyl], were prepd. from intermediates such as II [R2 = H, N-protecting group; R3 = H, alkyl, cycloalkyl, O-protecting group, etc.; R4 = H, Cl] for use as antibacterial agents. Thus, the trifluoroacetate salt of cephalosporin III was prepd. via amidation of (7R)-7-amino-3-(4-chloromethyl-1,2,3-thiadiazol-5-yl)thio-3-cephem-4-carboxylate 4-methoxybenzyl ester hydrochloride with (Z)-2-(N-triphenylymethylaminothiazol-4-yl)-2-(triphenylmethoxyimino)acetate Na salt. The prepd. cephalosporins were tested against a wide spectrum of organisms including organisms which are resistant to .beta.-lactam antibiotics.

IT **189449-00-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cephalosporin antibiotics)

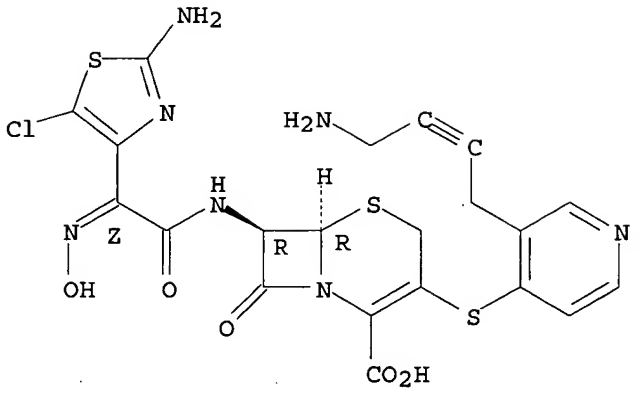
RN 189449-00-1 CA

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[3-(4-amino-2-butynyl)-4-pyridinyl]thio]-7-[[(2Z)-(2-amino-5-chloro-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

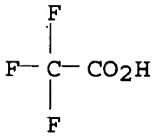
CRN 189448-99-5
CMF C21 H18 Cl N7 O5 S3

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

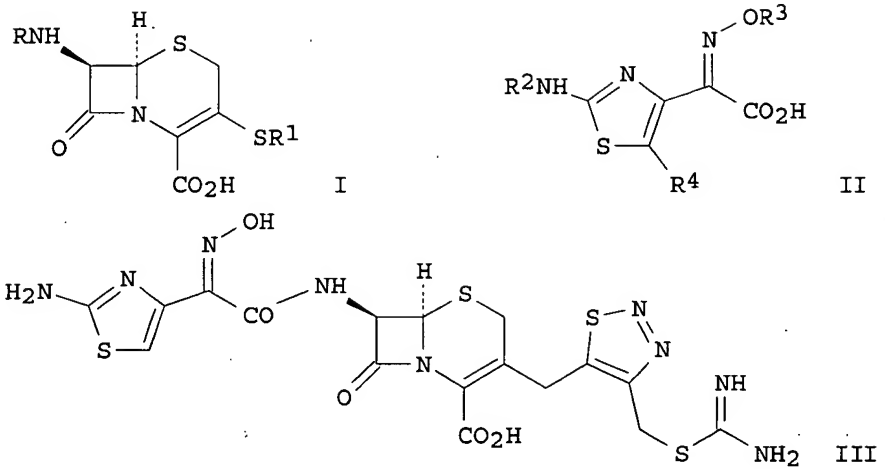


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:166063 CA
TITLE: Preparation of cephalosporin antibiotics
INVENTOR(S): Cho, In-Seop; Hecker, Scott J.; Glinka, Tomasz W.; Lee, Ving J.; Zhang, Zhijia J.
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: U.S., 38 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6025352	A	20000215	US 1997-937812	19970929

PRIORITY APPLN. INFO.: US 1997-937812 19970929
OTHER SOURCE(S): MARPAT 132:166063
GI



AB Cephalosporins (I) (R = acyl; R1 = heterocyclyl) were prepd. from intermediates such as (II) (R2 = H, N-protecting group; R3 = H, alkyl, cycloalkyl, O-protecting group, etc.; R4 = H, Cl) for use as antibacterial agents. Thus, cephalosporin III was prepd. via amidation of (7R)-7-amino-3-(4-chloromethyl-1,2,3-thiadiazol-5-yl)thio-3-cephem-4-carboxylate 4-methoxybenzyl ester hydrochloride with (Z)-2-(N-triphenylymethylaminothiazol-4-yl)-2-(triphenylmethoxyimino)acetate Na salt. The prepd. cephalosporins were tested against a wide spectrum of organisms including organisms which are resistant to .beta.-lactam antibiotics.

IT **189449-00-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cephalosporin antibiotics)

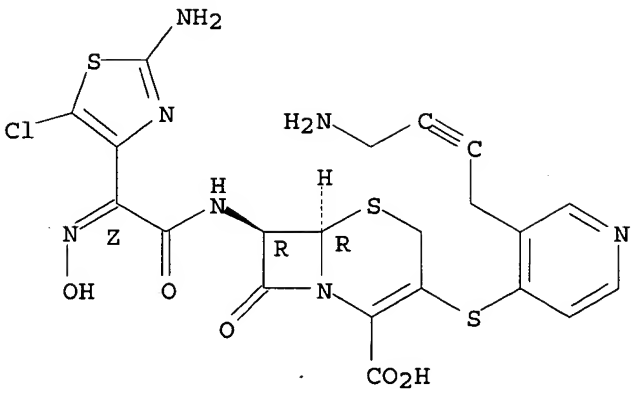
RN 189449-00-1 CA

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[3-(4-amino-2-butynyl)-4-pyridinyl]thio]-7-[[(2Z)-(2-amino-5-chloro-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

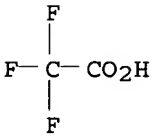
CRN 189448-99-5
CMF C21 H18 Cl N7 O5 S3

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

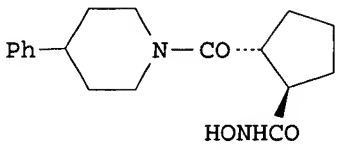


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:49888 CA
TITLE: Cyclic hydroxamic acids as metalloproteinase inhibitors
INVENTOR(S): Xue, Chu-Baio; Decicco, Carl P.; He, Xiaohua
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965867	A1	19991223	WO 1999-US13723	19990617
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2333554	AA	19991223	CA 1999-2333554	19990617
AU 9946923	A1	20000105	AU 1999-46923	19990617
EP 1087937	A1	20010404	EP 1999-930371	19990617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002518368	T2	20020625	JP 2000-554694	19990617

US 6429213 B1 20020806 US 1999-335086 19990617
PRIORITY APPLN. INFO.: US 1998-89557P P 19980617
US 1999-127599P P 19990402
WO 1999-US13723 W 19990617
OTHER SOURCE(S): MARPAT 132:49888
GI



I

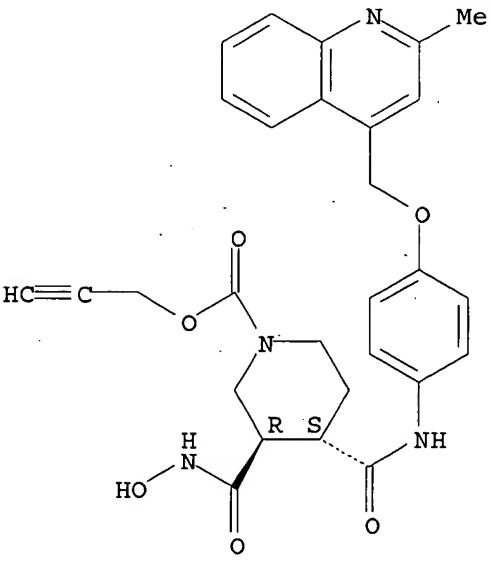
AB Title cyclic hydroxamic acids were prepd. which are useful as metalloprotease inhibitors (no data). Thus, trans-1,2-cyclopentanedicarboxylic acid was amidated with 4-phenylpiperidine and treated with NH2OH to give the hydroxamide I.

IT **252918-24-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic hydroxamic acids as metalloproteinase inhibitors)

RN 252918-24-4 CA

CN 1-Piperidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]amino]carbonyl]-, 2-propynyl ester, (3R,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



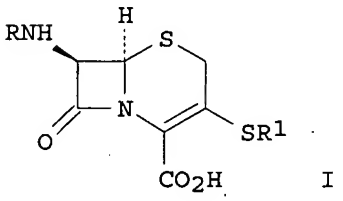
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:110111 CA
TITLE: Preparation of cephalosporin antibiotics
INVENTOR(S): Cho, In-seop; Hecker, Scott J.; Glinka, Tomasz W.;

Lee, Ving J.; Zhang, Zhijia J.
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: U.S., 31 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859256	A	19990112	US 1996-730040	19961011
CN 1204336	A	19990106	CN 1996-198934	19961011
CN 1066735	B	20010606		

PRIORITY APPLN. INFO.: US 1996-730040 A 19961011
OTHER SOURCE(S): MARPAT 130:110111
GI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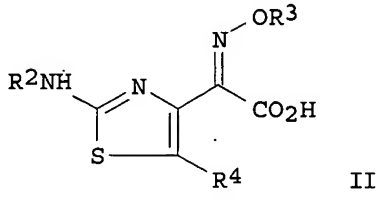
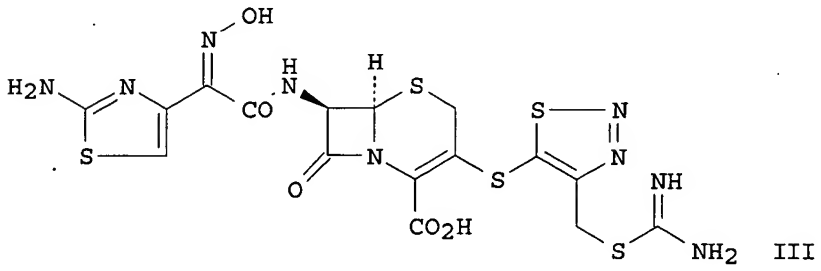

II


III

AB Cephalosporins I [R = acyl; R1 = heterocyclyl] were prepd. from intermediates such as II [R2 = H, N-protecting group; R3 = H, alkyl, cycloalkyl, O-protecting group, etc.; R4 = H, Cl] for use as antibacterial agents. Thus, cephalosporin III was prepd. via amidation of (7R)-7-amino-3-(4-chloromethyl-1,2,3-thiadiazol-5-yl)thio-3-cephem-4-carboxylate 4-methoxybenzyl ester hydrochloride with (Z)-2-(N-triphenylymethylaminothiazol-4-yl)-2-(triphenylmethoxyimino)acetate Na salt. The prepd. cephalosporins were tested against a wide spectrum of organisms including organisms which are resistant to .beta.-lactam antibiotics.

IT **189449-00-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cephalosporin antibiotics)

RN 189449-00-1 CA

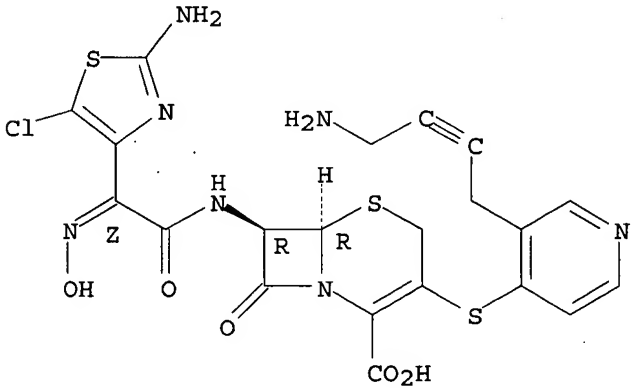
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[3-(4-amino-2-butynyl)-4-pyridinyl]thio]-7-[[(2Z)-(2-amino-5-chloro-4-

thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)-,
mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

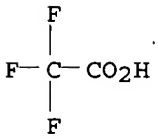
CRN 189448-99-5
CMF C21 H18 Cl N7 O5 S3

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

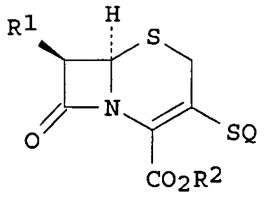
L10 ANSWER 15 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:330519 CA
TITLE: preparation and bactericidal activity of cephalosporin antibiotics
INVENTOR(S): Cho, In-Seop; Hecker, Scott; Glinka, Tomasz; Lee, Ving J.; Zhang, Zhijia J.
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713772	A2	19970417	WO 1996-US16349	19961011

WO 9713772		A3	19970605			
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
CA 2234255		AA	19970417	CA 1996-2234255		19961011
AU 9674417		A1	19970430	AU 1996-74417		19961011
AU 708676		B2	19990812			
ZA 9608617		A	19971021	ZA 1996-8617		19961011
EP 874854		A2	19981104	EP 1996-936406		19961011
EP 874854		B1	20011212			
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1204336		A	19990106	CN 1996-198934		19961011
CN 1066735		B	20010606			
BR 9611062		A	19990713	BR 1996-11062		19961011
JP 11513670		T2	19991124	JP 1996-515245		19961011
NZ 321135		A	20000128	NZ 1996-321135		19961011
US 6057312		A	20000502	US 1996-728233		19961011
US 6066630		A	20000523	US 1996-728232		19961011
US 6087355		A	20000711	US 1996-730042		19961011
EP 1059293		A1	20001213	EP 2000-202566		19961011
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
RU 2172317		C2	20010820	RU 1998-108533		19961011
AT 210666		E	20011215	AT 1996-936406		19961011
ES 2164924		T3	20020301	ES 1996-936406		19961011
TW 474935		B	20020201	TW 1996-85112602		19961015
NO 9801653		A	19980611	NO 1998-1653		19980408
HK 1017887		A1	20010921	HK 1999-102717		19990624
CN 1291611		A	20010418	CN 2000-126877		20000901
CN 1291612		A	20010418	CN 2000-126885		20000901
PRIORITY APPLN. INFO.:				US 1995-5389P	P	19951012
				EP 1996-936406	A3	19961011
				WO 1996-US16349	W	19961011

OTHER SOURCE(S): MARPAT 126:330519

GI



I

AB Synthesis of (7R)-7-(acylamino)-3-(arylthio)-3-cephem-4-carboxylic acids I [R1 = H2N, PhCH2CONH, (Z)-PhCH(=NOR3)CONH, (Z)-(un)substituted thiazol-4-yl CH(=NOR3)CONH; R2 = H, CHPh2, CH2C6H4-4-OMe; R3 = H, (un)substituted alkyl, (un)substituted heterocycle; Q = (un)substituted pyridyl, (un)substituted thiazolyl, (un)substituted thiadiazolyl] or their pharmacol. acceptable salts is given. The invention also relates to novel intermediates useful for making the novel compds. of the present invention and to novel methods for producing the novel compds. and intermediate

compds. Thus, I (R1 = PhCH2CONH, R2 = H, Q = 4-isothioureidomethyl-1,2,3-thiadiazol-5-ylthio).CF3CO2H (II) is prepd. in 7 steps from 1,3-dichloroacetone and Et 3-mercaptopropionate by reaction with Et carbazate, cyclization of hydrazone to 1,2,3-thiadiazole, reaction with 4-methoxybenzyl (7R)-7-[(phenylacetyl)amino]-3-trifluoromethanesulfonyloxy-3-cephem-4-carboxylate, chlorination, reaction with thiourea and deesterification with F3CCO2H. Data is given for II and I for antibiotic activity against 16 organisms including organisms which are resistant to .beta.-lactam antibiotics and are useful as antibacterial agents.

IT **189449-00-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and bactericidal activity of cephalosporin antibiotics)

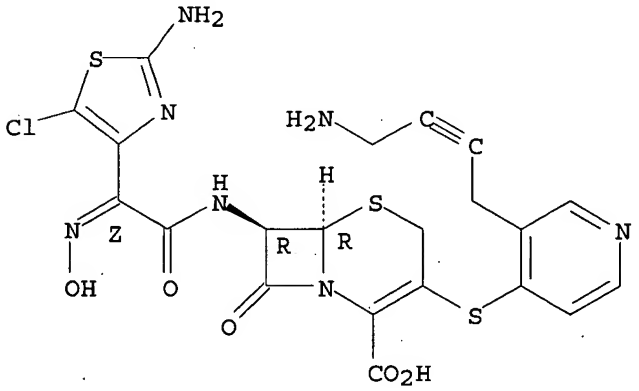
RN 189449-00-1 CA

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[3-(4-amino-2-butynyl)-4-pyridinyl]thio]-7-[[(2Z)-(2-amino-5-chloro-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

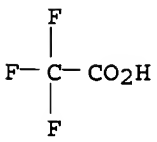
CRN 189448-99-5
CMF C21 H18 Cl N7 O5 S3

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L10 ANSWER 16 OF 16 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 117:26346 CA

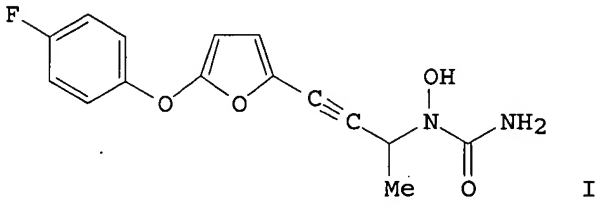
10/055,502

TITLE: Preparation of 1-[[(hetero)arylethynyl]ethyl]-1-hydroxyureas and analogs as lipoxygenase inhibitors
INVENTOR(S): Brooks, Dee W.; Stewart, Andrew O.; Kerkman, Daniel J.; Bhatia, Pramila A.; Basha, Anwer
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9201682	A1	19920206	WO 1991-US4911	19910711
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2087836	AA	19920126	CA 1991-2087836	19910711
AU 9184142	A1	19920218	AU 1991-84142	19910711
AU 647177	B2	19940317		
EP 540673	A1	19930512	EP 1991-915194	19910711
EP 540673	B1	19961016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05508861	T2	19931209	JP 1991-513716	19910711
JP 08019069	B4	19960228		
AT 144247	E	19961115	AT 1991-915194	19910711
ES 2095325	T3	19970216	ES 1991-915194	19910711
IL 98870	A1	19960804	IL 1991-98870	19910717
US 5476873	A	19951219	US 1994-229860	19940419
AU 9460774	A1	19940721	AU 1994-60774	19940428
AU 663441	B2	19951005		
US 5559144	A	19960924	US 1995-435399	19950505

PRIORITY APPLN. INFO.:
US 1990-558050 19900725
US 1991-684614 19910412
WO 1991-US4911 19910711
US 1993-971841 19930122
US 1994-229860 19940419

OTHER SOURCE(S): MARPAT 117:26346
GI



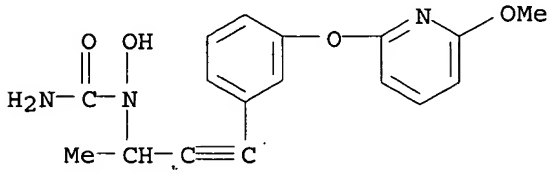
I

AB AC.tplbond.CB(CO)pN(OM)(CO)qR [I; B = bond, C1-12 alkylene; M = H, pharmaceutically acceptable cation or metabolically cleavable group; p .noteq. q = 0, 1; R = H, C1-12 alkyl, C3-8 cycloalkyl, NR1R2, with a proviso; R1 = H, C1-6 (hydoxy)alkyl, C1-6 (alkoxy)alkyl; R2 = H, HO, C1-6 (hydoxy)alkyl, C1-6 (alkoxy)alkyl, C2-8 alkanoyl, C1-6 alkyl(carbocyclic aryl), etc.; A = C5-20 alkyl, C3-8 cycloalkyl, (un)substituted carbocyclic aryl(oxy), etc.] or their pharmaceutically acceptable salts, useful as

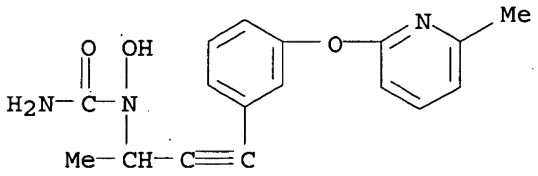
antiallergics and antiinflammatories, were prepd., e.g., by reaction of acetylenic alcs. AC.tplbond.CBOH with the novel bis(carboxyhydroxylamine) reagents R5O2CONHCO2R6 [R5 = (un)substituted phenyl(alkyl), C1-8 alkyl, etc.; R6 = (un)substituted Ph, NO2, halo]. Carbonate groups in the resulting acetylenic carbamates AC.tplbond.CBN(O2COR5)CO2R6 were cleaved and the intermediate N-hydroxyurethanes AC.tplbond.CBN(OH)CO2R6 converted by amines RNH2 to the title ureas. Thus, I (prepd. in 6 steps from 5-nitrofurfuraldehyde and FC6H4OH by the above method) had IC50 of 0.2 .times. 10-6M in an in vitro assay for 5-lipoxygenase inhibition.

IT **141579-75-1P 141579-77-3P 141580-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as lipoxygenase inhibitor)

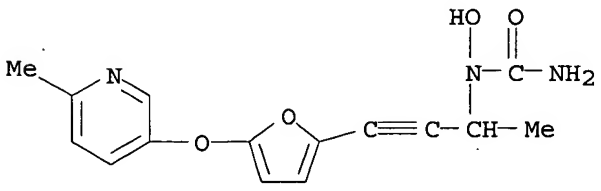
RN 141579-75-1 CA
CN Urea, N-hydroxy-N-[3-[3-[(6-methoxy-2-pyridinyl)oxy]phenyl]-1-methyl-2-propynyl]- (9CI) (CA INDEX NAME)



RN 141579-77-3 CA
CN Urea, N-hydroxy-N-[1-methyl-3-[3-[(6-methyl-2-pyridinyl)oxy]phenyl]-2-propynyl]- (9CI) (CA INDEX NAME)



RN 141580-16-7 CA
CN Urea, N-hydroxy-N-[1-methyl-3-[5-[(6-methyl-3-pyridinyl)oxy]-2-furanyl]-2-propynyl]- (9CI) (CA INDEX NAME)



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10/055,502

Executing the logoff script...

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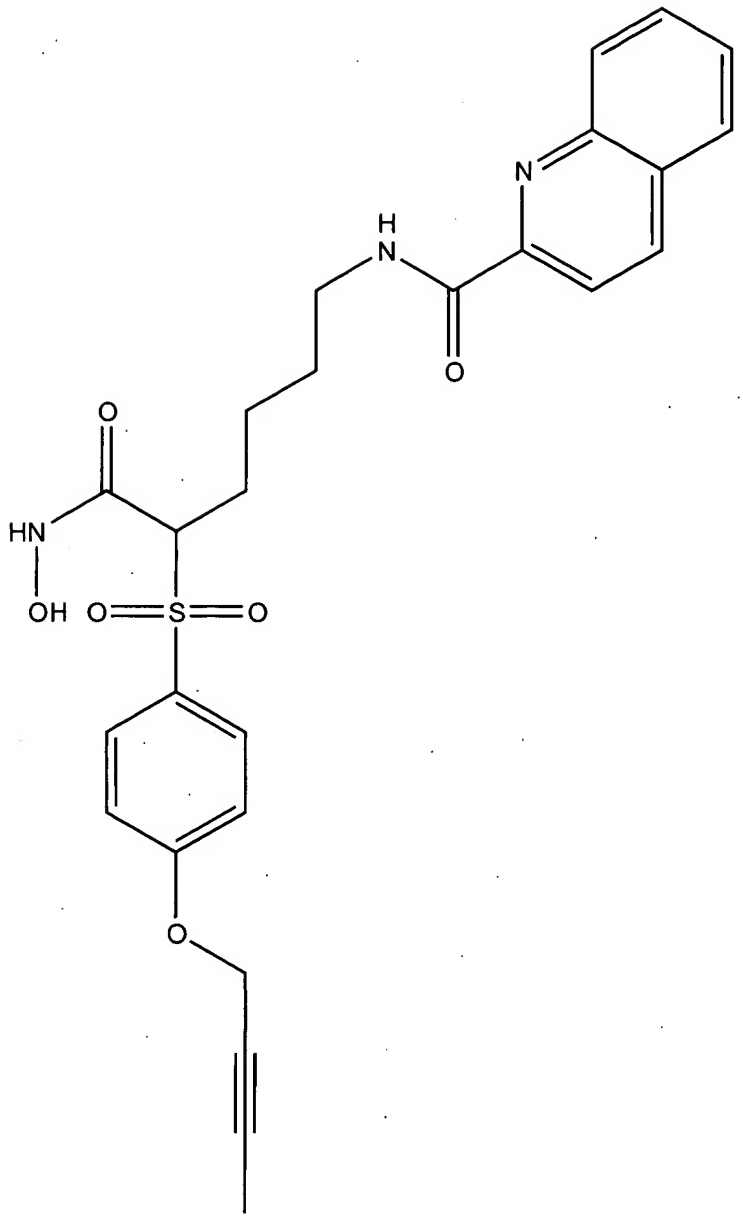
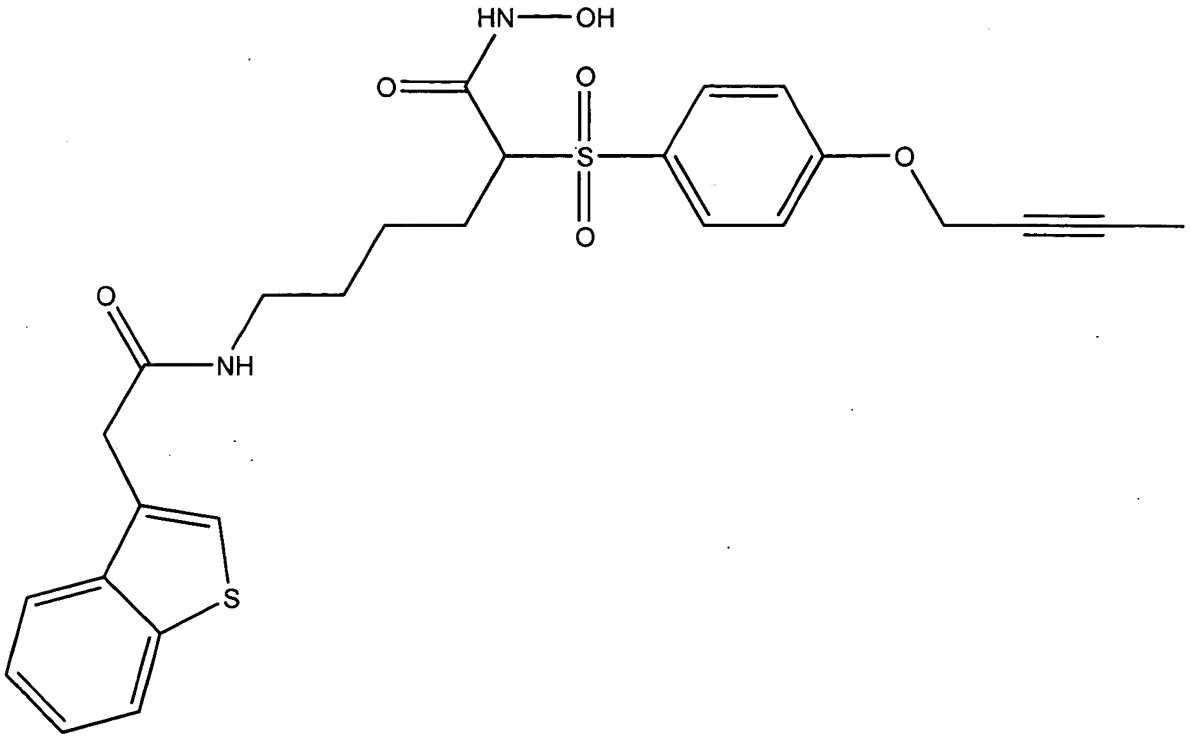
STN INTERNATIONAL LOGOFF AT 10:49:54 ON 14 MAY 2003



quinoline-2-carboxylic acid [5-(4-but-2-ynyloxy-benzenesulfonyl)-5-hydroxycarbamoyl-pentyl]-amide



6-(2-benzo[b]thiophen-3-yl-acetylamino)-2-(4-but-2-ynyloxy-benzene-sulfonyl)-hexanoic acid hydroxyamide